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Organophosphorus Compounds

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Preface

The organic chemistry of phosphorus compounds is in its second century. Yet no significant and comprehensive coverage of the subject was attempted until 1938, when V. M. Plets wrote his *Organic Compounds of Phosphorus*. Although Plets made an attempt to cover the entire field in his book, it was not sufficiently detailed to enable the reader to locate the numerous phosphorus-containing substances individually. Of even more importance, the book, being written in Russian, had limited usefulness for chemists in general.

My book was written in the hope of filling a significant gap in the chemical literature, the absence of any treatment of the general aspects of the organic chemistry of phosphorus. The first of its kind for English-speaking chemists, this book covers the considerable body of information accumulated in the decade since the publication of Plets' book in Moscow. In writing my book I took the position of an organic chemist rather than that of a biochemist. Consequently, the text was planned for convenient location of the available methods of preparing various compound types, with appended lists of known substances in each type, with lists of the principal physical properties of individual substances, and with proper references to the original literature. In compiling the book I made use of the chemical literature that had appeared until January 1949. The several significant additions made in the course of the following year, that is up to January 1950, are found in the Appendix, which follows the general plan of the body of the book.

Each chapter has this general plan. The brief introductory statement is followed by the compilation of the methods of synthesis that are applicable to the particular class of compounds. Each type of synthesis is labeled with a Roman numeral, which is reproduced immediately after the structural formula of each compound in the compound tabulations. The transformations that do not involve the phosphorus atom are, as a rule, of such a nature as to be readily apparent to an organic chemist. Such cases are indicated directly in the compound tabulations. The synthetic section of each chapter is followed by a summarization of the general physical and chemical features of the particular class. Exceptions to the general trend are indicated.

The present lack of a universally adopted system of nomenclature of organophosphorus compounds made it necessary to keep the use of specific names of compounds to a minimum in order to avoid possible

conflict with future usage. The plan of nomenclature in this book, largely for classes of compounds, differs somewhat from the several systems now in use. It does away with some class names that have been needlessly perpetuated and, I believe, it brings into closer relationship several compound types set apart by the current practices. The names of the discoverers, or of the principal contributors, connected with the major methods of synthesis are given in parentheses following the discussion of the chemistry involved in the particular procedure.

I wish to consider my book a tribute to two pioneers in the field of phosphorus chemistry. The foundation work of Professor August Michaelis, in many respects the father of the organic chemistry of phosphorus, is our link with the past. The fine experimental and theoretical work of Professor A. E. Arbuzov is our link with the future.

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August 1950

Contents

1. Introduction	1
2. Phosphines and Related Compounds	10
3. Halophosphines	42
4. Halophosphine Halides and Phosphonyl Halides	58
5. Quaternary Phosphonium Compounds	78
6. Tertiary Phosphine Oxides, Sulfides, and Selenides	98
7. Phosphinous, Phosphonous, and Phosphonic Acids, Their Sulfur Analogs and Esters	121
8. Phosphites and Thiophosphites	180
9. Phosphates, Halophosphates, and Thio Analogs	211
10. Compounds with Phosphorus to Nitrogen Bonds	278
11. Quasi-Phosphonium Compounds	325
12. Derivatives of Anhydro Acids	333
Appendix	355
Index	371

Introduction

Organic compounds of phosphorus have been in existence at least since the beginnings of life on this planet. Such substances were probably prepared artificially for the first time in the Middle Ages, when alchemy was popular and when man, free of the fetters of either tradition or experimental techniques, engaged himself with reactions that might be called heterogeneous, in the fullest sense.

The scientifically planned study of these compounds may be regarded as having begun in the early part of the nineteenth century. In this respect, the esterification of dehydrated phosphoric acids with alcohols represents, in all probability, the first piece of research in this field. This interpretation dates the beginning of this branch of organic chemistry as 1820, with the pioneer credit to Lassaigne. Some two decades later phosphine derivatives were prepared by Thenard and others, and in the succeeding years of the nineteenth century the chemistry of organophosphorus compounds developed at a rather rapid pace. This development continued with increased vigor in the opening decades of the present century, as may be witnessed by the voluminous literature on the subject in its various aspects.

A general survey of the course of such development shows that the greatest amount of effort has been expended in the purely synthetic aspects. Although the theoretical problems have been attacked by many workers in the field, no generally applicable monolithic foundation has been constructed, and it is only in the most recent years that we begin to find the more generalized approach to the various aspects of the subject. Not only is the sheer bulk of the experimental data impressive, but the contradictory nature of a considerable portion of the data presents a formidable task for a logical presentation. So far as possible, the questionable or contradictory pieces of evidence are pointed out and discussed in this book.

The literature contains the evidence of the work of many hundreds of chemists who made great and small contributions to our present knowledge of the organic chemistry of phosphorus. By far the greatest bulk of this work represents the academic dissertations of students of relatively few major investigators, who remained true to this branch

of chemistry for considerable periods of time. It is perhaps impossible to name one single man as the outstanding contributor to the field; this is certainly true if we consider all the possible facets of the subject.

The purely synthetic aspect of organophosphorus compounds has most certainly been emphasized by Professor Carl Arnold August Michaelis, who during his long and illustrious lifetime was unquestionably the outstanding leader in this subject not only in Germany but in all the world. In a period of some four decades he and his students were responsible for a vast amount of synthetic work and for the development of at least the master-stroke outlines of almost all the methods of preparation in use at present. The work of Michaelis gave a foundation for the chemistry of phosphorus compounds, a foundation that persists even to this day, when a number of his experimental techniques and procedures have been rendered obsolete by newer developments. The degree of obsolescence, however, is remarkably small when we consider the span of time involved, beginning with the late 1860's.

The period that overlaps the latter stages of activity of the Michaelis school and extends to the present time developed a number of pioneering investigators. Among them is the founder of the present Russian school of phosphorus chemistry, Professor Aleksandr Erminingel'dovich Arbuzov, who may be regarded as a worthy successor to Michaelis both for his elaboration of methods of synthesis and for his very early attempt at unification of the basic principles of reactions of phosphorus compounds. Particularly significant has been his elaboration of the nature of isomerization reactions of derivatives of trivalent phosphorus. His son, B. A. Arbuzov, has been a rather frequent contributor to this field, although the major interests of the younger Arbuzov lie in the field of terpene chemistry, which also attracted the attention of his father some thirty years ago. Professor Arbuzov's daughter, Irina, was beginning to make her mark in this branch of chemistry when her career was cut short.

Although it is a simple matter to name the titular heads of the German and the Russian schools, this cannot be done for the very productive galaxy of British scholars. We should mention the names of Frederick G. Mann and Walter C. Davies in connection with the extended studies of the phosphines. The name of Professor Alexander R. Todd is closely linked with the development of several new methods of phosphorylation and with elegant pioneer syntheses in the realm of substances related to nucleic acids—syntheses that culminated in the first authentic preparation of adenosine triphosphate a short time ago.

As we examine the literature in this field, its trend is apparent. The investigations along lines leading to the biological and the biochemical

aspects have been multiplying at a great rate. The importance of the phosphorus derivatives in the normal and abnormal manifestations of life phenomena is becoming more and more apparent. It is primarily for the purpose of summing up the significant results of a century's progress and, it is hoped, to assist the developments along the lines indicated above that this book was conceived. Although much remains to be done in the matter of improved synthetic methods, the organic chemistry of phosphorus finds itself at the present time on the threshold of a great future, and it is rapidly finding many important expressions and applications of both an industrial and a scientific nature. It is in the curious position of a stepchild that is becoming a favorite. The stepchild position occupied for many decades is apparent from the infrequent references to phosphorus compounds in the standard textbooks of organic chemistry.

This book has been designed to fit the requirements of an organic chemist and to enable him to locate the suitable methods of preparation of the various types of organic compounds of phosphorus. Only synthetically available substances of rather firmly established constitution have been considered for this compilation, and the numerous biological materials that cannot be assigned permanent structures for lack of synthetic evidence have been omitted. The purely biochemical aspects are multiplying and changing so rapidly that an attempted summary of them at this time would become obsolete even during the course of its preparation.

A serious obstacle to the compilation of this type lies at present in the confusion and the lack of nomenclature uniformity in phosphorus derivatives. Although work on the development of a system is in progress, its adoption lies some years in the future. For this reason, the make-up of this book has been altered in some respects to atone for this deficiency as far as possible. The tabulations of known compounds that appear in each chapter have been constructed in the sense of structural formulas that will not become obsolete. The arrangement of these tabulations in order of progression of complexity eliminates the need for an extensive index of names, as the individuals can be readily found by scanning the compound tables, or at least as readily as if there were a list of names. This feature is also an aid in keeping the size of the book to a reasonable magnitude.

Each chapter has this general plan. The brief introductory sentence is followed by the compilation of the methods of synthesis that are applicable to the particular class of compounds. Each type of synthesis is labeled with a Roman numeral, which is reproduced immediately after the structural formula of each compound in the compound tabula-

tions. The transformations that do not involve the phosphorus atom are, as a rule, of such a nature as to be readily apparent to an organic chemist. Such cases are indicated directly in the compound tabulations. The synthetic section of each chapter is followed by a summarization of the general physical and chemical features of the particular class. Exceptions to the general trend are indicated.

Although specific names have been kept to a minimum, for the reason given above, it has been necessary, of course, to make some use of them. The plan adopted in this book differs in some respects from the current practice. It does away with some class names that have been needlessly perpetuated and, it is believed, it brings into closer relationship several compound types set apart by present practice. The names of the discoverers, or of the principal contributors, connected with the major methods of synthesis are given in parentheses following the discussion of the chemistry involved in the particular procedure.

The nomenclature used in this volume is illustrated by the following examples of class and individual names. Customary radical symbols are used for the abbreviated notation in the text.

RPH₂, R₂PH, R₃P. Phosphines; primary, secondary, tertiary. EtPH₂—ethylphosphine; EtBuPhP—ethylbutylphenylphosphine. The rather closely related compounds in which a fourth organic radical is linked to phosphorus, probably by semipolar bond, retain the present name of phosphinemethylenes.

RPX₂, R₂PX. Mono- and dihalophosphines. MePBr₂—methyl-dibromophosphine; Ph₂PCl—diphenylchlorophosphine.

RPX₄, R₂PX₃, R₃PX₂. Alkyl-(aryl)phosphorus halides. EtPCl₄—ethylphosphorus tetrachloride; Bu₂PCl₃—dibutylphosphorus trichloride.

RP(O)X₂, R₂P(O)X. Phosphonyl halides; primary, secondary. EtP(O)Cl₂—ethanephosphonyl dichloride; EtPhP(O)Br—ethylphenylphosphonyl bromide. Sulfur analogs are named by using the prefix thiono: MeP(S)Cl₂—methanethionophosphonyl dichloride.

R₄PX. Quaternary phosphonium compounds. Et₄PCl—tetraethylphosphonium chloride; MeEt₃POH—methyltriethylphosphonium hydroxide.

R₃PO. Tertiary phosphine oxides. Pr₃PO—tripropylphosphine oxide. The sulfur and selenium analogs are the sulfides and the selenides, respectively.

RP(O)(OH)₂, R₂P(O)OH. Phosphonic acids; primary, secondary. PhP(O)(OH)₂—benzenephosphonic acid; EtPhP(O)OH—ethylphenylphosphonic acid. The esters are named phosphonates: MeP(O)(OEt)₂—diethyl methanephosphonate. The sulfur analogs are named by using

the prefix thio as a noncommittal term in the free acids and in their salts; esters in which there is ample evidence for semipolar link of sulfur to phosphorus are characterized by thiono prefix.

RPO₂H₂. Phosphonous acids. PhPO₂H₂—benzenephosphonous acid. The esters are named phosphonites. The sulfur analogs bear the thio prefix.

R₂POH. Phosphinous acids. These compounds are listed as acids provisionally until more direct evidence is secured about their behavior. Et₂POH—diethylphosphinous acid. The esters are named phosphinites. The sulfur analogs are named by using the thio prefix.

(RO)PX₂, (RO)₂PX. Mono- and dihalophosphites. EtOPCl₂—ethyl dichlorophosphite. Sulfur analogs bear the thio prefix: EtSPBr₂—(S)-ethyl dibromothiophosphite.

ROPO₂H₂, (RO)₂POH, (RO)₃P. Phosphites; primary, secondary, tertiary. (EtO)₂POH—diethyl phosphite; (PhO)₃P—triphenyl phosphite. The sulfur analogs are named by using the thio prefix.

ROP(O)X₂, (RO)₂P(O)X. Halophosphates. MeOP(O)Cl₂—methyl dichlorophosphate. The sulfur analogs use the thio prefix for compounds with RS links; the P(S) link is designated by the thiono prefix.

ROP(O)(OH)₂, (RO)₂P(O)OH, (RO)₃PO. Phosphates; primary, secondary, tertiary. (MeO)₂P(O)OH—dimethyl phosphate; (BuO)₃PO—tributyl phosphate. The sulfur analogs use the thio prefix unless definite proof of the thiono structure is on hand.

The amides of the phosphorous and phosphoric acids are named in the manner indicated by the examples below. EtOP(O)(NHMe)₂—ethyl N,N'-dimethyldiamidophosphate; (PhNH)₂P(O)OH—N,N'-diphenyldiamidophosphate; Et₂NPCl₂—dichloro-N,N-diethylamidophosphite; (EtNH)₃PO—N,N',N''-triethyl phosphoric triamide; (EtNH)₃P—N,N',N''-triethyl phosphorous triamide.

Imides of phosphorus acids. EtOP:NMe—ethyl N-methylimidophosphite; PhOP(O):NEt—phenyl N-ethylimidophosphate. The sulfur analogs are named as described above.

RP(O)(NR₂)₂, R₂P(O)(NR₂). Phosphonamides. PhP(O)(NH₂)₂—N,N'-diethyl-benzenephosphondiamide.

R₂PNR₂. Phosphinamides. Et₂PNPr₂—N,N-dipropyl-diethylphosphinamide.

R₃P→NR. Phosphinimines. Ph₃PNEt—triphenylphosphine-ethylimine.

Quasi-phosphonium compounds. Substances analogous to the true phosphonium compounds and to the phosphorus halides, but containing ester or amide groups. PhOPCl₄—phenoxyphosphorus tetrachloride; (MeO)₂Et₂PI—dimethoxydiethylphosphorus iodide.

Derivatives of anhydro acids of phosphorus are named in the conventional method after the names of the acids. $(\text{EtO})_2\text{P}(\text{O})\text{OP}(\text{O})(\text{OEt})_2$ —tetraethyl pyrophosphate; $(\text{MeO})\text{PO}_2$ —methyl metaphosphate.

The system illustrated above departs from the common usage in the American literature by omission of "phosphinic" acids— $\text{R}_2\text{P}(\text{O})\text{OH}$. The derivation of the acids is made from phosphoric and phosphorous acids by replacement of hydroxyl groups by the radicals. The use of the term "chlorophosphonate" by the British for chlorophosphates is rejected as highly undesirable.

LABORATORY WORK WITH PHOSPHORUS COMPOUNDS

The laboratory workers in this branch of chemistry should be aware of possible toxicity of some apparently innocuous compounds. Although phosphorus and phosphines have been known to be toxic for many years, only recently have the toxic properties of a great number of organic derivatives of phosphorus been appreciated. Specifically, esters of pyrophosphoric acid, fluorophosphates, some of the alkylaryl phosphates and thionophosphates, and probably other classes have a profound influence on living organism, shown mostly by a powerful anticholinesterase activity. The effects of such compounds upon the nervous system make it definitely advisable to take adequate precautions before taking liberties with exposures to substances with unknown physiologic action. Halides of phosphorus are acute respiratory irritants and should be handled only in a room that is adequately ventilated.

The usual precautions concerning anhydrous conditions should be taken in work involving the use of phosphorus halides and compounds with anhydro structures. In addition, a number of reactions of phosphorus derivatives are apparently catalyzed or modified by traces of moisture; the entire course of such reactions may be significantly altered unless moisture is rigorously excluded. Trivalent phosphorus derivatives must be handled with especial care because they possess a high order of reactivity both in hydrolytic and additive reactions.

Many syntheses involve several consecutive reactions that are best conducted under reduced pressure with agitation. In such case the recourse to a rubber-sealed vacuum stirrer, which does not seem to the uninitiated to be a reliable device, is highly recommended. Most of the esters are relatively stable to water at low temperatures, and the usual water-washing techniques may be used for purification procedures. Azeotropic drying of such washed solutions may be utilized in most

instances. Particularly useful is such drying at water-pump vacua, which permit drying at substantially room temperature, when such solvents as petroleum ether or benzene are used.

Although the usual analytical procedures for the estimation of phosphorus may be found in the usual textbooks and literature sources, and as such lie outside the scope of this book, the conversion of the organic derivatives to the inorganic phosphate deserves mention. The peroxide bomb fusion serves admirably for all the common classes of compounds. The procedure given recently by Bachofer and Wagner² is typical of the modern techniques. A rapid and convenient precipitation of the "yellow precipitate" in citrate medium may also be recommended.⁸ Occasional specimens of highly resistant substances, usually members of highly substituted phosphonic acids and tertiary phosphine oxides, do not give adequate decompositions; such compounds have been fairly successfully decomposed by heating with concentrated sulfuric acid and 30% hydrogen peroxide.⁸

The common method of structure confirmation by molecular refractivity is often used. The constants evaluated by Jones, Davies, and Dyke are usually employed.⁵ A recent paper by Kabachnik⁶ gives a much more extensive set of data. The constitutive effects are reflected in the atomic values for phosphorus, when 1.643 is used for the oxygen atom in carbon-oxygen-phosphorus link, 2.211 for semipolar oxygen in the phosphoryl group, 6.336 for chlorine, and 9.598 for bromine in phosphorus halides. The atomic values for phosphorus are 7.04 for phosphites and halophosphites, 3.75 for phosphates and halophosphates, and 4.27 for phosphonates and phosphonyl halides. The atomic values of phosphorus are unaffected by substitution of an RO group for halogen. The somewhat less frequently used parachor has been investigated extensively and recently by B. A. Arbuzov and co-workers. The group standard values are 101.27 for tertiary phosphites, 93.7 for primary phosphonates, 115.45 for dialkyl phosphites assuming a monomer structure, and 229.8 assuming a cyclic dimer structure (most likely); tertiary phosphates give 119.9 and tertiary thionophosphates 149.8 for the group standard values.¹

It should be noted that in many classes of organophosphorus compounds we find mixtures that are inseparable by fractional distillation, owing to proximity of boiling points. Such mixtures are common in replacements of halogens by OR groups, in which partial as well as complete replacement may occur. Such crossover points are also found in pairs of di- and trialkyl phosphites. Notable examples are diethyl chlorophosphite and triethyl phosphite, and di-*n*-butyl phosphite and tri-*n*-butyl phosphite.

Any proper understanding of the behavior of organophosphorus compounds must have a foundation of sound knowledge of the mechanisms of reactions of such substances in the primitive forms. Unfortunately, knowledge is lacking for the entire subject. Perpetuation of the use of the "simple" formulas for many of the primary reagents in discussions of their reactions does nothing to promote knowledge. For this reason, for instance, many reactions, particularly those involving the hydrolytic and alcoholic attacks on substances with phosphoryl or thionophosphoryl groups, are being treated widely at this time as simple radical substitution reactions, whereas the actually observable facts lie in direct contradiction to such representations. Although much experimental material must be collected under controlled conditions in order that a proper attack on the mechanisms of such reactions can be made, a careful sifting of the material on hand with due consideration of the conditions under which the work was done is in order. There is little value, for instance, in repeating the results reported on the reactions of esters of phosphorous acid studied before 1905-1906, before the classical work of Arbuzov, because all the earlier preparations were unknowingly contaminated with a variety of by-products.

In the elucidation of reactions of phosphorus compounds a proper weight must be given to the well-demonstrated additive properties of the phosphoryl and thionophosphoryl groups. They are not likely to remain inert in hydrolytic or alcoholic reactions, and reaction representations based on simple cleavage of the divalent oxygen to phosphorus bonds are not adequate; this is a rather common failing in discussions of hydrolyses of esters and anhydrides in the phosphorus family. Although much stress is laid in this book on the probability of formation of quasi-phosphonium compounds in the common reactions of compounds containing the above-mentioned groups, it is not felt that this stress was undue. One of the greatest problems to be solved is the adequate physical or chemical means for the identification of complexes of phosphorus compounds, complexes that may arise in the primary stages of reactions. It must be realized that even the relatively simple esters of polyacids in this family have not found a clean-cut method of specific identification.

Adequate discussions of the reaction mechanisms of organophosphorus compounds are nonexistent largely for lack of any truly comprehensive studies along the modern lines of such investigations. Only a recent review with comments by Kabachnik may be recommended; it, however, covers but a minute fraction of the field.⁷ An admirable review of the inorganic aspects of phosphorus chemistry, which may find much use

in interpretation of some of the organic reactions, has been written by Dyatkina.⁴

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Phosphines and Related Compounds

PHOSPHINES

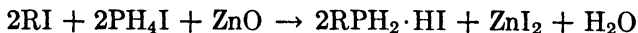
Phosphines are derivatives of trivalent phosphorus in which one (or more) phosphorus to carbon link exists, with the remaining phosphorus valences (if any) being bound by hydrogen.

METHODS OF PREPARATION

It should be noted that the phosphines must be prepared and handled with due regard for their affinity for oxygen. Therefore, in careful work, air should be excluded by the usual methods. Exclusion of air is imperative in working with the lower alkyl members, particularly those having unsaturated radicals. As a rule, the aryl members are fairly stable in this respect.

I. Reaction of alkyl halides with phosphonium iodide and zinc oxide

Heating a mixture of an alkyl halide (usually the iodide) with phosphonium iodide in a sealed vessel to 100 to 180° for several hours leads to the formation of a complex mixture of primary, secondary, and tertiary phosphines, as well as phosphonium salts. Although the individuals can be separated fairly readily, a reaction of this type is not suitable for high-yield syntheses of a particular phosphine. Obviously, the equation of the reaction cannot be drawn up in toto. The formation of the primary type may be shown by:



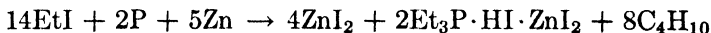
and the formulations for the secondary and the primary types may be regarded as a continuation of the above reaction, with progressive replacement of the phosphorus-hydrogen bonds of phosphonium iodide by organic radicals. Addition of water to the cooled reaction mixture liberates some by-product phosphine and the primary phosphine, both of which are very weak bases. The secondary and the tertiary phosphines are liberated by addition of alkali and are then separated by

fractional distillation.^{25, 66, 66, 67, 68, 70, 122} Dry ammonia may be used conveniently for the liberation step.²⁵ Modern low-temperature vacuum distillation techniques can be used with advantage in the separation of the lower members.²⁵ Powdered zinc may be substituted for the zinc oxide.⁹⁶ (Hofmann.)

IA. Reaction of phosphonium iodide with alcohols or ethers.

Heating phosphonium iodide in a sealed vessel with an excess of an alcohol or an aliphatic ether to 120 to 180° for several hours results in formation of tertiary phosphines, accompanied by much larger amounts of phosphonium iodides (R_4PI).^{45, 63, 64, 134} The phosphine forms a double salt with hydrogen iodide and must be liberated by addition of alkali.

IB. Heating alkyl iodides with phosphorus and zinc. When the above mixture, containing a substantial excess of the iodide, is heated in a sealed tube for several hours to 150° a poor yield of the tertiary phosphine is obtained. Much of the product mixture is composed of the quaternary phosphonium compounds. The phosphine is liberated from its salt by alkali, as mentioned earlier. A mixture of hydrocarbons (partly olefinic) is also formed. The partial equation for the reaction with ethyl iodide may be formulated.⁶¹



II. Reaction of white phosphorus with alkyl iodides in alkali

Addition of alkyl iodides to white phosphorus in aqueous sodium hydroxide results in the formation of a spectrum of phosphine derivatives, similar to that obtained in I. The products are isolated by distillation or are oxidized in situ to the corresponding acids and phosphine oxides.⁴ The yields of the individual members are usually below 20 to 30%. The reaction probably proceeds through the formation of alkali salts of the lower acids of phosphorus, with the formation of the primary phosphine being shown by the over-all equation. (Auger.)

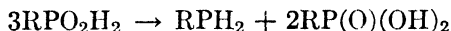


III. Reaction of alcohols with phosphorus

Heating white phosphorus with aliphatic alcohols in a sealed vessel for several hours to 250° results in formation of the entire series of phosphine derivatives (see Sections I and II), in addition to which appreciable amounts of their oxidation products (phosphonic acids, etc.) are also isolated. Ethylphosphine has been obtained in 20% yield, which appears to be the maximum to be expected.⁷ (Berthaud.)

IV. Oxidation reduction of phosphonous and phosphinous acids

When a phosphonous acid, RPO_2H_2 , is subjected to heat (100° or somewhat above suffices in most instances) the resulting mixture contains large amounts of the corresponding primary phosphine and phosphonic acid. Although the actual yields of these products, especially of the phosphines, are far below the theoretical, this reaction has usually been presented in the form of an oxidation-reduction process, which may be shown by the following equation.^{109, 116} (Michaelis.)



This reaction has been applied to several aliphatic compounds, but it has found its widest application in the aromatic series, although, as mentioned above, the yields of the phosphines are very unsatisfactory. The phosphinous acids undergo this reaction much more readily, in accordance with the other characteristics of these substances, and yield the secondary phosphines and the corresponding phosphonic acids. The precise mechanism of the reaction is not known, but it may involve structure considerations of these acids, which are discussed in Chapter 7, under reactions of these acids.

Ordinarily, the reaction is performed in such a manner that the requisite acids are formed in situ from the corresponding halophosphine derivatives. The halo- or dihalophosphine is hydrolyzed by addition to water, alcohol, or, best, dilute alkali, and the resulting solution is subjected to distillation (in inert atmosphere, for obvious reasons). The use of alkali is particularly effective with the secondary halophosphines, although the yields under any conditions are not high.⁹⁶ Among the halophosphines, the iodo derivatives appear to be most effective.^{91, 108} Aqueous sodium carbonate appears to be the most satisfactory form of alkali in this reaction.¹³¹ (Michaelis; Plets.)

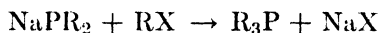
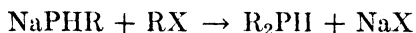
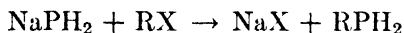
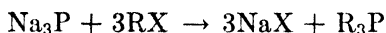
V. Reaction of phosphonium iodide and aliphatic polyhalides

When a mixture of phosphonium iodide and zinc oxide is heated with chloroform, some methylphosphine is obtained; heating with ethylene bromide yields some ethylphosphine. The yields of these products, under conditions analogous to those cited in Section I, are poor, and the usual product mixtures are formed.⁶⁹ (Hofmann.)

VI. Reaction of alkyl halides with compounds having a phosphorus to metal linkage

Although this reaction, in its many variations, has been known for over a century, its development has been unusually slow. It is potentially among the most economical reactions suitable for the synthesis

of phosphine derivatives. The reaction, in its general aspect, may be regarded as an improvement on the reactions taken up in Sections I, II, and V, inasmuch as it restricts the degree of substitution to the number of phosphorus to metal bonds present in the starting material. Thus metal phosphides (or alloys) and metal derivatives of primary and secondary phosphines react readily with alkyl halides to give good yields of the desired phosphines, with cleavage of the corresponding metal halides, and a similar reaction takes place with metal derivatives of phosphine. The typical reactions are shown below.

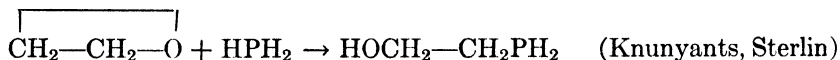


The metals used in the reaction are usually sodium or potassium,^{1,82,153} although calcium¹⁴⁹ and zinc¹¹ have been used for reactions of a type shown in the first equation. The sodium or potassium intermediates may be prepared by the action of the metal on the appropriate phosphine in liquid ammonia, with appropriate precautions to repress substitutions beyond the desired limit (for phosphines having more than one hydrogen).⁸² The products obtained in this manner, however, are not completely free of nitrogen, and a more clean-cut reaction is secured when triphenylmethylsodium is made the source of the metal.¹ In this case, even phosphine may be converted satisfactorily to a pure monosodium derivative, when the reaction is carried out in ether, with the triphenylmethylsodium being slowly added to an ether solution of phosphine, through which a rapid stream of phosphine is passed. Sodium and potassium derivatives of the primary and the secondary phosphines have been prepared in inert solvents, such as benzene or toluene, by direct reaction of the metal, usually at elevated temperatures for the higher members.^{153,155} The alkyl halides used in this reaction have ranged from chlorides to iodides; aryl halides do not appear to be suitable, at least under the fairly mild conditions used thus far. The halide is added to a suspension of the metal derivative in an organic solvent (usually *in situ*) and the reaction is completed by warming the mixture (the higher members require a period of reflux). The metal halide is removed by filtration or by washing with water, and the product is isolated in the usual manner from the organic layer. Yields of over 50% may be expected with careful techniques. An obsolete procedure, largely of historic significance, was the source of the first synthetic phosphines. Methyl chloride, passed over heated calcium phosphide,

gave a complex mixture of phosphines, the non-homogeneity being due undoubtedly to the quality of the phosphide used.¹⁴⁹ (Thenard; Albers, Schuler; Walling.)

VII. Reaction of phosphine with olefin oxides

Although phosphine does not react with ethylene oxide under the conditions of normal pressure and room temperature, a reaction does take place in an autoclave at 100°, preferably in dry ether. The product mixture, comprising a 10 to 12% yield in a reaction of 20 hours' duration, contains primary, secondary, and tertiary phosphines, which form as a result of ring opening of the oxide by the proton of the phosphine. The formation of the primary product, for instance, may be shown as:



The secondary derivative is obtained in the smallest amounts, as a rule; this may be accounted for by the disproportionation that appears to be most effective among the secondary derivatives of phosphorus, in general. Propylene oxide reacts similarly, forming 2-hydroxypropyl derivatives.⁸⁷ The reaction may be significantly improved for the preparation of the primary derivative, if sodio-dihydrogenphosphorus (that is, monosodium derivative of phosphine) is used. In this case, phosphine may be introduced into a solution of the requisite amount of sodium in liquid ammonia, after which ethylene oxide is passed into the solution. The solvent is allowed to evaporate, and the residue, after treatment with a little water, is fractionated; yields up to 70% have been obtained.⁸⁷

VIII. Reaction of phosphine with acyl halides

Acyl halides, which have a substantial degree of electronegative substitution, react with phosphine, apparently, by substitution and form acylphosphines, which are crystalline substances extremely easily broken down by water to the free phosphine. Chloroacetyl and di- and trichloroacetyl chlorides react in this manner to form phosphines of type $\text{RCO} \cdot \text{PH}_2$.^{16, 146} In an apparently analogous reaction, cyanogen chloride forms cyanophosphines from primary phosphines.²³ (Cloe; Steiner.)

IX. Reaction of phosphines with alkyl halides

Phosphine itself reacts rather unsatisfactorily with alkyl iodides on being heated in sealed tubes, with or without zinc iodide,^{41, 64} and forms a spectrum of derivatives (see Section I) in poor yields. However,

somewhat better results are secured when primary or secondary phosphines are used as starting materials in sealed tube reactions above 100°. ⁶⁸ The products are formed essentially by progressive substitution of the hydrogen atoms by the radicals and are obtained in the form of salts (HI), from which they are liberated by alkali. (Hofmann.)

X. Reaction of phosphonium iodide with carbonyl compounds

Phosphonium iodide reacts with aldehydes at elevated temperatures in sealed tubes to yield hydroxyalkyl derivatives. Usually the entire spectrum of derivatives is obtained, with the individual yields being quite unsatisfactory. ⁵⁰ The products may be isolated in the usual manner. The reaction bears a certain resemblance to the reaction of olefin oxides (Section VII), although it is reported that ethylene oxide under these conditions yields only ethylene iodide. ⁵⁰ The first step of the substitution may be shown as follows. (Girard.)



XA. Reaction of carbonyl compounds with phosphine in the presence of hydrogen chloride. Carbonyl compounds, usually aldehydes, react with phosphine in a rapid stream of hydrogen chloride to yield hydroxyalkyl derivatives in a manner suggestive of the reaction taken up above. It is possible that phosphine is activated by coordination to the carbonyl group to become able to form a substance analogous to phosphonium halide with hydrogen chloride, which then reacts in the manner indicated above. As a rule, the reaction is conducted in a stream of both gases, and the result of such procedure is the predominant formation of the higher substitution products, essentially phosphonium salts. Thus pyruvic acid forms the trisubstitution product, which, however, cannot be easily isolated in its original (trihydroxyalkyl) form, but undergoes a dehydration reaction to the corresponding anhydride. ¹⁰⁴ (Messinger, Engels.)

XI. Reduction of halophosphines

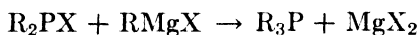
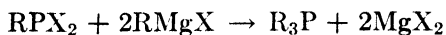
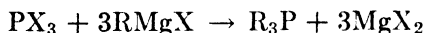
The usual "wet" methods of reduction are essentially useless for the reduction of halophosphines. There is no information on reduction by methods that would involve the use of solvents that are without action on the halophosphines, that is, the use of catalytic procedures in inert solvents.

However, a rather indirect reduction of diphenylchlorophosphine to diphenylphosphine has been achieved by the reaction of the former with zinc at elevated temperature, followed by treatment with water. ³⁹ The mechanism of the reaction is uncertain and may involve a Würtz-

type coupling, followed by hydrolytic cleavage, or the reaction may proceed by the way of a zinc derivative, Ph_2PZnCl , which yields the product with hydrolytic attack. (Dörken.)

XII. Reaction of Grignard reagents with halogen derivatives of trivalent phosphorus

The reaction considered in this section is the most convenient laboratory method for the synthesis of tertiary phosphines. The starting materials may be phosphorus trihalides, halophosphines, and dihalophosphines. Usually, the chloro derivatives are used because of their greater availability. The reaction proceeds by the usual substitution process and results in formation of the tertiary phosphines having either identical or different radicals. In this respect the reaction is similar to the syntheses discussed in Section VI.



The reactions are usually conducted in ether and are completed, after the addition of the halide, by refluxing. Two types of procedures have been used for the isolation. Either the entire reaction mixture may be subjected to vacuum distillation⁵⁶ or the mixture is given the usual hydrolytic treatment with ammonium chloride solution, followed by distillation of the organic layer,^{30,35} with the products being obtained either by distillation in vacuo or by crystallization (usual for the aryl derivatives). The first procedure was reported to give up to 70% yield of triethylphosphine, although it does not seem to be a desirable process for the higher boiling products. The aqueous process is most commonly used. The aryl derivatives are usually obtained in very good yields (up to 70 to 80%); the aliphatic derivatives, however, are formed in extremely variable yields. The derivatives of the primary halides give the best yields as a rule, although the higher members are formed in yields that are not at all satisfactory (substantially below 30 to 40%). Alkyl halides with branched chains and, especially, secondary alkyl halides give either extremely poor yields or essentially no detectable amounts of the desired products.³⁵ This takes place even under the best conditions known: a large excess of the Grignard reagent. It is possible that the poor yields in such cases, especially with the higher primary halides, may be caused by poor reactivity of the products of intermediate degrees of substitution, in which event the use of solvents of higher boiling point than ether may be an effective cure. An investi-

gation of the precise nature of the reaction mixtures actually obtained in such cases should be of great interest.

It is obvious that failure to use an appropriate excess of the Grignard reagent can result in the formation of by-products of acid type after the hydrolytic treatment.

Although the normal Grignard reagents are customarily used, it has been shown that the magnesium derivatives of nitrogen heterocyclics can take the place of the usual RMgX -type reagents. Reactions of such magnesium compounds derived from indole and related substances yield the normally expected tertiary phosphines of the R_3P types. However, because of the tautomeric nature of the magnesium derivatives, some phosphorus-nitrogen bound derivatives are also formed. These may be regarded as a form of amidophosphites. They are discussed in Chapter 10. They differ from the carbon-phosphorus phosphines by their inability to form nitrogen-silver derivatives. In addition, they are usually unstable to warm aqueous alkali and can readily be separated from the normal carbon-phosphorus phosphine derivatives.¹²¹

A small amount of information exists about the possible use of organolithium compounds in place of the Grignard reagents. Thus phenyldichlorophosphine reacts smoothly with organolithium compounds, such as *p*-aminophenyl-lithium, to yield the expected tertiary phosphine in a reaction similar to those obtained with the Grignard reagents.⁴⁸



The necessary lithium derivative can be made in situ by a reaction of exchange type in dry ether at low temperature (-60°C) between butyl-lithium and *p*-bromoaniline. The reaction proper is conducted by mixing the dichlorophosphine with the solution of the lithium derivative and refluxing the mixture briefly. The product is isolated by usual hydrolytic treatment and extraction of the basic phosphine with dilute hydrochloric acid, from which it is liberated by alkali.

It is interesting to note that, whereas an expected spectrum of derivatives of all possible degrees of substitution is obtained from Grignard reagents and phosphorus pentachloride, yields of appreciable amounts of tertiary phosphines have been reported.⁵⁹

Another interesting variation is the formation of triphenylphosphine in 60% yield from triphenyl phosphite and an excess of phenylmagnesium bromide.⁴⁹ In this reaction, in which phenol is formed as a by-product of the substitution, after hydrolysis, the formation of phosphonic esters or phosphine oxides is avoided by the use of an aryl ester.

An obvious extension of this reaction to the two-ended Grignard reagents in reactions with dihalophosphines has been used to prepare

cyclic phosphines, in which phosphorus forms a part of a polymethylene cycle.⁶² (Grignard; Hibbert; Pfeiffer; Davies *et al.*)

XIII. Reaction of organozinc compounds with halogen derivatives of trivalent phosphorus

This reaction is a rather obsolescent variant of the Grignard reaction discussed above. It was used extensively before the introduction of the Grignard reagents in reactions of essentially the same types as were covered in the previous section. The zinc derivatives of R_2Zn type are used in a manner similar to the Grignard reagents, with the added precautions necessary in operations with these pyrophoric materials. The reactions are conducted in ether solution, as a rule, and those involving the use of phosphorus trihalides are usually run with cooling in the initial addition step because of the highly exothermic reaction.^{24, 160} The products are liberated from the zinc halide double salts, which form in the reaction by treatment with alkali, usually potassium hydroxide solution.^{13, 24, 71} The reaction may be performed in a modified manner by the simultaneous action of the alkyl halide, halophosphine, and zinc. In this case, of course, the reaction might proceed in a manner similar to a Würtz reaction, or the formation of the organozinc compounds may be the intermediate process. The yields from the organozinc reagents are not superior to those obtained by the more convenient Grignard reagents. (Hofmann, Cahours.)

XIV. Thermal decomposition of quaternary phosphonium halides

Quaternary phosphonium halides decompose on strong heating, with the loss of one radical and the halogen atom, to yield tertiary phosphine derivatives. If the original compound contains several different radicals, the usual order of separation from phosphorus results in the formation of phosphines with mixed radicals. Since the order of separation is not absolutely exclusive and the variation of bond strengths is not very great among the various radicals, a degree of inhomogeneity may be normally expected in the products, which form, in such cases, mixtures of the several possible tertiary phosphines. They form in accordance with the general expression given below:



The order of radical cleavage is: ethyl, benzyl, methyl, propyl, iso-amyl, phenyl, in descending order.⁴³

The reaction is essentially a dry distillation at temperatures above 200°, as a rule. The products are isolated by distillation, usually in vacuo.^{18, 43, 44, 84}

Tetrachloromethylphosphonium chloride yields the corresponding trichloromethylphosphine by treatment with aqueous alkali in a radical departure from the more conventional quaternary compounds.⁵⁷ Some tertiary phosphine may be obtained by the reaction of triphenylmethylsodium with quaternary phosphonium halides.¹⁷

The use of the quaternary phosphonium compounds does not appear to have significant advantages over the more convenient Grignard procedure, especially if the preparation of the necessary starting materials is considered. The over-all yields are usually quite good, although, in mixed derivatives, the yield of any particular compound may be rather unsatisfactory. (Hofmann; Ingold *et al.*)

XV. Reaction of organic halogen derivatives with halogen derivatives of trivalent phosphorus, with metallic sodium

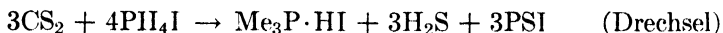
This form of the conventional Würtz reaction has been used rather often in the preparation of tertiary phosphines with aryl radicals, although derivatives of the aliphatic type may be used similarly. Either phosphorus trihalide or halophosphines may be used. If the first, the symmetric products are formed. If the second, we may obtain products of the symmetric type or those with mixed radicals, depending upon the starting materials. In the simplest form the reaction may be illustrated by the equation shown below.



Usually the chlorides are used for the phosphorus derivatives. The organic halides may be chloro, bromo, or iodo derivatives, although customarily the first two are preferred. The reaction is conducted at reflux in an organic solvent (frequently ether is used in laboratory preparations) for several hours, until the decomposition of sodium metal is evidently complete. Occasionally, this requires 24 hours, or even longer periods. The yields are usually satisfactorily high, generally ranging upward of 50% of theory, especially when agitation is used. The products are isolated as usual, after filtration or washing.^{111, 114, 118} The higher halides, which are rather sluggish, are best used in higher-boiling solvents, such as benzene, and may be activated by antimony trichloride, added in a small amount to the mixture.^{161, 162} (Michaelis.)

XVI. Reaction of carbon disulfide with phosphonium iodide

In this rather unique reaction carbon disulfide is heated in a sealed tube to 150 to 180° with phosphonium iodide for several hours. The resulting mixture yields some trimethylphosphine, after treatment with potassium hydroxide solution to liberate the product from its salt with hydrogen iodide.⁴⁰ The over-all equation is given below.

**XVII. Reaction of phosphorus trichloride with dialkylanilines**

When N,N-dialkylaniline is heated with phosphorus trichloride to 130 to 160° some trisubstitution occurs, with the attachment of the phosphorus atom taking place at the para position (this point has not been absolutely verified). If a substantial excess of the amine is used (6 moles per mole of the trichloride), rather good yields of the tertiary phosphines are obtained.^{9,133} Similarly, the replacement of the amine excess by pyridine is effective.⁸⁸ In these cases the excess amine or pyridine act as binding agents for the by-product, hydrogen chloride. The reaction of this type was observed in mixtures containing aluminum chloride,¹¹⁹ but it was found soon afterward that the catalyst is completely unnecessary. The reaction in this instance may be shown by the following equation. (Bourneuf; Raudnitz.)



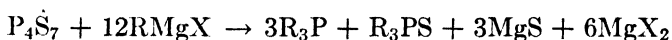
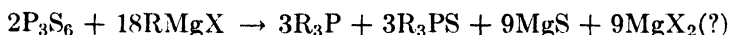
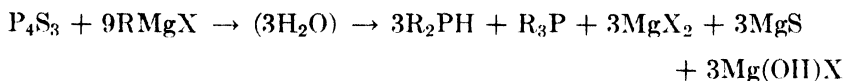
However, variable quantities of the products of mono- and disubstitution are formed concurrently. These form, after the usual treatment of the mixture with aqueous alkali, the corresponding acidic derivatives of the type of phosphonous or phosphinous acids. These are separated by alkali solubility, or in the latter type by organic solvents, after steam distillation of any residual amines.

XVIII. Reaction of Grignard reagents with phosphorus sulfides

Lower sulfides of phosphorus react with Grignard reagents and yield a complex mixture of products of neutral and acidic types, after the usual hydrolytic treatment.⁹⁶ Although these sulfides of phosphorus are not well characterized as to their true individuality and exact structure, the nature of the reaction must be such as to provide for the progressive cleavage of phosphorus to sulfur bonds until the individual molecule of the product is liberated. The possible nature of the reaction is discussed further in Chapters 6 and 7, in which the formation of the concurrent products, tertiary phosphine sulfides and thiophosphonic acids, is taken up. Whereas phosphorus pentasulfide yields

products of the latter types predominantly, the lower sulfides of phosphorus give rise to appreciable yields of secondary and tertiary phosphines. The investigation of this reaction is in very early stages, and it is not practicable to assign specific experimental conditions at this time.

It is possible to write numerous theoretically balanced equations in which the final products are accounted for qualitatively.⁹⁶ As a matter of fact, the yields do not correspond to theory by wide margins, and the formulation of such equations, without taking into account the actual structures of the sulfides and the mechanism of the attack on them, seems to be rather pointless. Typical equations may be set up as:



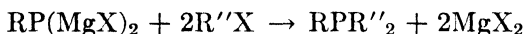
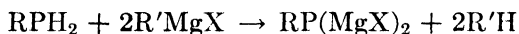
The reaction is conducted by adding the Grignard reagent to the phosphorus sulfide (usually exothermic) and refluxing the mixture for 10 to 12 hours; usual hydrolytic treatment with water is followed by the recovery of the phosphines from the organic layer by distillation. With P_4S_3 , yields of up to 20% of secondary aliphatic phosphines and up to 40% of diphenylphosphine (the only aryl derivative studied thus far) may be obtained, when 8.5 to 16 moles of the Grignard reagent are used. The amounts of the tertiary phosphines, their sulfides, and quaternary phosphonium salts rise with an increase of the proportions of the Grignard reagent above 9 moles. When $\text{P}_3\text{S}_6(?)$ is used, the secondary phosphines are largely absent and the tertiary phosphines are produced in moderate yields, lower than those obtained with P_4S_3 because the excess of the Grignard reagent serves to form the quaternary salts. With P_4S_7 the secondary phosphines are absent, and yields of 40% of tertiary phosphines are obtainable. As such, these reactions do not appear to have any points of advantage over the usual Grignard- PCl_3 reaction in the synthesis of tertiary phosphines. All the phosphorus sulfides yield variable amounts of acidic derivatives, principally of the thio- and polythiophosphonic and thiophosphinous classes. (Malatesta.)

XIX. Reaction of dialkylzinc compounds with phosphine

When dialkylzinc compounds are allowed to react with phosphine and the reaction mixture is treated with an alkyl iodide, moderate yields of tertiary phosphines are formed.⁴¹ The reaction proceeds, in all prob-

ability, by intermediate formation of phosphorus-zinc derivatives that react with alkyl iodides to form the final products. The tertiary phosphines form the zinc iodide double salts, from which they are liberated by the usual treatment with alkali.⁴¹ This reaction is a forerunner of the more modern reaction discussed below. (Drechsel.)^{46, 58}

XIXA. Reaction of Grignard reagents with compounds containing a phosphorus to hydrogen bond. Compounds such as the primary and the secondary phosphines, that is, substances with a phosphorus to hydrogen linkage, react smoothly with Grignard reagents. The products that form in the primary reaction are substances resulting from substitution of these hydrogen atoms by the MgX radical. As such, they enter into smooth reaction with reactive organic halides, such as acyl halides, to form tertiary phosphines in which one or two radicals are supplied by the organic halide.⁸¹ It is unfortunate that very little information is on hand about the limitations of this reaction, for at first glance it should be one of rather wide scope. The typical equation is given below. (Job, Dusollier.)



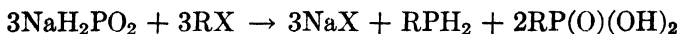
XX. Displacement of arsenic from arsines by phosphorus

Heating triphenylarsine with phosphorus to 300° results in the formation of triphenylphosphine and arsenic, apparently by a displacement process. The scope of the reaction is not known.^{90, 147} (Schönberg.)

XXI. Reaction of sodium hypophosphite with alkyl halides

Although phosphines have not been isolated as such from this reaction, there is little doubt about their formation. The products were oxidized immediately upon formation to phosphonic acids.¹³⁰

Addition of alkyl bromides or, preferably, iodides to a solution of sodium hypophosphite in dilute alcohol results in the formation of primary phosphines in moderate yields, along with the secondary and tertiary phosphines in low yields. The main reaction may be shown by:



The primary, secondary, and tertiary phosphines are separated from the by-product phosphonic acids by distillation. As expected, bromobenzene fails to react. Curiously, ethyl chloroacetate yields a small amount of methylphosphine.¹³⁰ (Plets.)

GENERAL CHARACTERISTICS

Phosphines are very reactive substances, a characteristic of all derivatives of trivalent phosphorus. They possess the rather unpleasant characteristic odor of phosphine and are probably rather toxic, as a class; certainly, the lower members produce toxic symptoms after moderate exposures.

Although all phosphines are subject to oxidation, the primary and the secondary phosphines, especially those containing the lower aliphatic radicals, are outstanding in their affinity for atmospheric oxygen. The aromatic derivatives, especially the tertiary forms, are rather stable in this respect, but are readily attacked by a variety of oxidizing agents. The lowest oxidation products of primary phosphines that have been isolated are the phosphonous acids, RPO_2H_2 ; stronger means of oxidation give the very stable phosphonic acids, $\text{RP}(\text{O})(\text{OH})_2$. The secondary phosphines form the corresponding secondary phosphonic acids, $\text{R}_2\text{P}(\text{O})\text{OH}$, although sometimes it has been possible to detect or to isolate the intermediate derivatives: phosphinous acids of type R_2POH . The tertiary phosphines form the corresponding oxides, R_3PO .

The additive properties of trivalent phosphorus are similarly displayed by the reaction of phosphines with sulfur. Although little is known about the products of sulfur addition to primary phosphines, in general, it has been shown that phenylphosphine reacts with sulfur, especially at elevated temperatures, to form a sulfide, PhPSH_2 , which may be regarded as an unusual form of a thiophosphinous acid; the product is discussed in Chapter 7. In addition, some crystalline product, m. 138° , is formed; this is an even lower addition product of composition $\text{Ph}_3\text{P}_3\text{S}$. Since this substance yields diphenylphosphonic acid on oxidation, it is probable that two phenyl radicals are already attached to one phosphorus atom in its molecule. The true constitution of the material is unknown.¹¹⁵ Secondary phosphines add sulfur readily with the formation of secondary dithiophosphonic acids, $\text{R}_2\text{PS}_2\text{H}$, after the treatment of intermediate polysulfides with aqueous reagents.^{13, 72, 96} Tertiary phosphines add sulfur with the formation of corresponding sulfides, R_3PS ; selenium and tellurium act in a similar manner.^{13, 36} Although the oxidation of tertiary phosphines is an apparent chain reaction, going probably through the peroxide,¹⁵⁰ there is no mechanism information on the sulfur addition reaction. The sulfur addition via organic disulfides, such as dibenzoyldisulfide, is also a characteristic of the tertiary phosphines.¹³⁷

Phosphines react vigorously with halogens. Usually, unless the necessary precautions of dilution and temperature control are followed,

the phosphines with phosphorus to hydrogen bonds are totally destroyed. Under controlled conditions hydrogen replacement takes place and halophosphines are formed.¹⁵⁴ Tertiary phosphines add halogens to form rather unstable dihalides, R_3PX_2 .^{79, 92, 111, 112, 114, 120} The hydrogen atoms of phenylphosphine are readily replaced in its reaction with phosgene, which occurs at elevated temperatures and yields carbon monoxide and hydrogen chloride as by-products;¹¹³ phenyldichlorophosphine is readily obtained in this manner. Tertiary aromatic phosphines are also capable of accepting two halogen atoms (chlorine) in the course of prolonged heating with the chlorides of trivalent phosphorus, antimony, arsenic, and bismuth; this reaction may be a form of disproportionation.¹⁴ The scope of this reaction is undetermined; for instance, tri-*o*-xenylphosphine does not react, although the para isomer reacts rather readily.^{161, 162}

Phosphines as a class are bases; the degree of basicity is dependent upon the degree and the nature of substitution. Thus, methyl-, dimethyl-, and triethylphosphines form a steadily ascending scale of basicity, in contrast to the corresponding amines. This is made possible by the relatively large dimensions of the phosphorus atom, which permits the maintenance of the normal valence angles in tertiary aliphatic phosphines.^{10, 66, 142} As was noted in the discussion of synthetic methods, the primary phosphines form salts that are readily hydrolyzed by water, whereas the salts of the secondary and the tertiary phosphines are more stable and are decomposed only by alkaline reagents. The triarylphosphines represent the lower end of the basicity scale, and their salts are usually decomposed by water. In the mixed aryl-alkyl derivatives the basic properties are of intermediate strength and are affected substantially by the groups present on the aromatic nuclei. Thus the substitution of alkyl groups in the ortho and para positions increases the basicity of the phosphines, but their basicity is not changed so profoundly as in the corresponding amines.²⁸ Introduction of 2-pyridyl groups in place of phenyl groups in triphenylphosphine produces an interesting series of phosphines in which the salt-forming properties of the nitrogen atom of the pyridine nucleus are affected by transmission through the heavy phosphorus atom. Salt formation takes place only at the nitrogen atoms and not on the phosphorus, which is substantially neutral.¹⁰¹

Phosphines react with alkyl halides and form the corresponding quaternary derivatives. The ease of such addition is roughly in accord with the basicity of the compounds; the relative difficulty of such a reaction with primary and secondary phosphines has been mentioned in the section on synthetic methods. However, the tertiary phosphines

in which the addition proceeds most readily display definite variation of reactivity in this respect, a variation that has been studied with various aromatic-aliphatic members. Generally, the rate of addition decreases rather rapidly with increased bulk of the radicals in both reagents. Although measurements of alkyl halide addition to trialkylphosphines in acetone solution indicate an equilibrium reaction that does not go to completion,²⁹ it is probable that in this case the completion is prevented by coordination complex formation between the phosphines and the solvent. The rate of addition of alkyl halides to phosphines of type ArPAlk_2 has been investigated in some detail, as it has been for the Alk_3P ^{59,105} and Ar_3P types. Generally, the formation of quaternary salts, unlike the basicity, is affected by steric factors as well as polar factors. The polar factor is well shown in the series of meta and para substituted phosphines, in which the steric factor is absent. The descending order of reactivity can be given as *p*-ethyl-, *p*-methoxy-, *p*-tolyl-, plain phenyl-, *p*-chloro-, *p*-bromo-, *p*-iodo-, *m*-nitro-, *p*-nitro-.³¹ The reactivity of the phosphines is higher than that of arsines or amines.^{28,31} This is also well shown in the series of phenylpyridylphosphines, mentioned earlier; thus these substances form only a monomethiodide. It is of interest to note that, in this instance, the pyridyl groups are rather readily replaced by the methyl group on heating with an excess of methyl iodide, in a process of the usual decomposition of the phosphonium salts.¹⁰¹

Phosphines as a class tend to form a large variety of double or complex salts with metal derivatives; this ability is usually best shown in the tertiary phosphines. The adducts with carbon disulfide have received much attention since the earliest studies. The nature of the adduct of the secondary phosphines is not clear. The primary substance obtained from carbon disulfide and phenylphosphine has the over-all composition of $(\text{PhPH} \cdot \text{CS})_2\text{S}$, and, since some hydrogen sulfide is evolved in the process, the unisolated initial material appears to be a coordination product between the two reactants. Treatment of the above sulfide with alkali yields thiocarboxylic derivatives of the phosphine, which are not well established in respect to precise structure but appear to be compounds of the general type $\text{PhPH}(\text{CS}_2\text{M})$. Reaction of the original sulfide with chlorine yields products in which the carbon disulfide residue is detached, which speaks for the coordinate nature of the adduct. The products are halophosphines and thiophosphonyl chlorides, with thiophosgene being a prominent by-product.¹¹³ The adducts of the secondary phosphines are similar.⁶⁵ The adducts of the tertiary phosphines, which have received most of the attention,^{34, 36, 55, 61, 68, 77, 79, 145, 159} appear to be either linked by a semipolar phos-

phorus to sulfur bond³⁴ or more likely represent a form of an "inner salt" in which a phosphorus to carbon bond exists as well as a polar bond between the phosphorus (positive pole) and a sulfur atom.³⁶ The adducts are only moderately stable and dissociate in a regular manner in the expected order of decreased stability dependent upon the nature of the substituents on the phosphine radicals. Such a series was studied in the ArPAlk₂ type of phosphines.³⁶ The adducts can form methiodides, which are quaternary salts displaying conductivity of the order given by alkali salts.⁷⁹

The double salts of phosphines with metal halides have been examined largely in connection with problems of stereochemistry. Such are the adducts with mercury halides,^{77, 89, 97, 100} as well as those of cadmium,^{97, 100} gold,^{100, 102, 126} palladium,^{97, 99} silver,^{99, 102} nickel,⁷⁹ cobalt,⁷⁹ copper,^{3, 102} platinum,⁷⁹ zinc,^{19, 145} boron,¹²⁸ and tin.¹⁹

It is of interest to note some reactions that take place only if some form of complex salt intermediate is postulated. Thus triphenylphosphine, which is unaffected by air, is readily oxidized in the presence of AlCl₃⁹⁵ or disulfides;¹³⁷ similarly, triphenylphosphine does not react, per se, with phenylmagnesium bromide, phenyl-lithium, or bromobenzene, although the formation of the corresponding quaternary phosphonium derivatives proceeds very readily in such systems in the presence of oxygen or aluminum chloride.^{38, 47, 95} Similarly, the same phosphine forms the oxide at essentially room temperature in mixtures with water and diphenyldisulfide; the "removal" of oxygen from the water molecule is most remarkable and obviously proceeds by the way of complex formation.¹³⁷

Highly unsaturated compounds, especially those with cumulative unsaturation, form complexes with tertiary phosphines. It is probably correct to regard these substances as coordination compounds since the majority of them undergo decomposition under rather mild conditions. Such compounds are the adducts with azides and diazo compounds,^{5, 143, 145} which are discussed in Chapter 10, phosphinomethylenes, which are discussed later in this chapter, and the adducts of ketenes and isothiocyanates,^{55, 145} as well as the colored adducts with such reagents as maleic anhydride, itaconic anhydride, and *p*-benzoquinone, which form readily with triphenylphosphine.^{138, 140} A study of such adducts, essentially of the phosphinimine type with a semipolar link between phosphorus and nitrogen, has been made, in which the effect of substituents on the aromatic groups in the phosphine residue upon the strength of polarity of the semipolar bond was investigated and showed the expected decrease of such polarity as the electron density at the phosphorus was increased.^{15, 98} If the polarity of the bond is

high, the reaction of the phosphine with Chloramine-T hydrate results in the formation of phosphinimine hydrates, presumably containing a hydroxyl at the phosphorus atom; if the polarity is reduced, normal phosphinimines are formed.⁹⁸

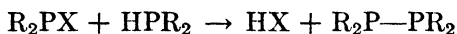
The reactions in which the phosphorus-linked hydrogens of primary and secondary phosphines are replaced by alkali metals or the inorganic radicals of the Grignard reagents have been mentioned in sections VI, XIX, and XIXA, devoted to the synthesis of phosphines. Many of the common substitution reactions of organic chemistry cannot be used with phosphines because of the nature of the trivalent phosphorus. Thus nitrations and halogenations cannot be conducted without alteration of the phosphines into derivatives of higher valences of phosphorus. However, lithium may be introduced in the meta position in triphenylphosphine by the exchange reaction between butyl-lithium and either triphenylphosphine or *m*-bromophenyldiphenylphosphine; the reaction is slow.⁴⁷

Although claims were made some years ago that substances with five radicals covalently bound to phosphorus may be obtained by the reaction of Grignard reagents with compounds of type R_3PX_2 ,⁵¹ it was shown later that the claim was in error.⁸ Although phosphorus may be able to retain five groups in intermediate substances in the course of a reaction transition period, stable pentacovalent products are unlikely. The phosphinomethylenes, discussed in the following pages, are not compounds of this type, as they contain a semipolar link that is amply demonstrated by their reactions.

BIPHOSPHINES AND RELATED PRODUCTS

Very little information exists about the substances in this section. The pertinent references are to be found in the lists of compounds at the end of this chapter.

The compounds of types R_2P-PR_2 may be obtained by the reaction of secondary halophosphines with secondary phosphines by elimination of hydrogen halide.



The compounds of type $RP:PR$ are similarly obtained from the dihalophosphines and primary phosphines. These substances are also obtainable by a Würtz-type reaction of active metals with halophosphines of appropriate types.

Substitution of phenylarsine for phenylphosphine in the above reaction yields a mixed product: phosphoarsenobenzene, PhAs:PPh , which disproportionates on heating into the phosphobenzene, PhP:PPh .

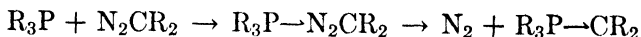
Because of the relatively weak phosphorus to phosphorus bond, the compounds of these types are readily cleaved by chemical attack with water, oxygen, halogens, and hydrogen halides. The products are the expected derivatives of the corresponding phosphines.^{39, 115}

A number of ill-defined products have been obtained from the interaction of phenyldichlorophosphine with small amounts of water and with phosphine. These substances are assumed to contain several phosphorus atoms per molecule and to produce on oxidation varying amounts of phosphonic acids. It does not seem profitable to speculate about the nature of these materials until their identity as individuals has been established.¹⁰⁷ (Michaelis.)

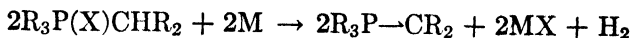
PHOSPHINOMETHYLENES

These substances are derivatives of phosphines in which the three organic radicals on the phosphorus atom are supplemented by a fourth group attached to the phosphorus by a semipolar bond. As a rule, these substances are poorly stable and are easily attacked. Thus water leads to the formation of tertiary phosphine oxides even under mild conditions. The compounds of this category are usually very brightly colored.

These substances have been obtained by thermal decomposition of the coordination compounds of tertiary phosphines and diazoalkanes.¹⁴⁵



They may be obtained, somewhat more readily, from quaternary phosphonium halides in which at least one hydrogen is present on a carbon bound to the phosphorus atom. The reagents suitable for the removal of halogen and hydrogen atoms in such an instance are several: butyl-lithium, triphenylmethylsodium, or molten alkali metals are commonly used.^{17, 123, 144} The 9-fluorenyl derivative of triphenylphosphine has been prepared by the use of alcoholic ammonia.¹²⁹ Preparations of these types are shown by:



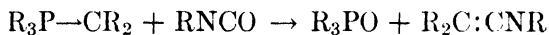
Because the phosphinomethylenes are extremely reactive their synthesis must be conducted under appropriate conditions, usually in a

free-radical apparatus. They add water, alcohols, and acids readily, and form the corresponding quaternary phosphonium compounds, that is, reversal of the second general method of synthesis.

Combined oxidative-hydrolytic attack, which occurs in contact with moist air, usually leads to cleavage of the substance into a tertiary phosphine oxide and a hydrocarbon. This reaction proceeds by the intermediate formation of the phosphonium hydroxide that undergoes the usual decomposition reaction.

Reaction with sulfur leads to a rapid formation of the tertiary phosphine sulfide and a thioketone, which suggests the mechanism of the reactions of tertiary phosphines with thioketones in the presence of air, discussed among the reactions of phosphines on the preceding pages.

Reaction with isocyanates proceeds to the phosphine oxides with concurrent formation of ketenimines.¹⁴⁵ (Staudinger.)



In leaving the subject of phosphines, we may mention some additional data of interest. Dissociation of phosphines, that is, cleavage of the constituent radicals, has not received much attention. In this connection it has been found that triphenylphosphine is transformed into benzene and phosphorus on being heated in hydrogen atmosphere, only at temperatures above 325°, thus showing greater stability than the arsenic, bismuth, or antimony compounds.⁷⁵ Although the reactions of tertiary phosphines with aluminum chloride, in which a complex is formed, have been mentioned earlier, it may be of interest to add that such complexes are able to react with aldehydes to form quaternary phosphonium salts.⁷³

The phosphines, as a class, have not found a significant field of application in the practical world. Although they may be used as intermediates for the synthesis of a great variety of phosphorus derivatives, the rather costly methods of preparation and, to some extent, the unpleasant physical characteristics of the members of this family undoubtedly have been the significant factors in this lack of exploitation. Phosphines, per se, have been suggested for applications involving antioxidant action, obvious from the chemical properties of the class. A minor, but interesting, use of triaryl members as analytical agents for detection of dienophylic agents, such as maleic anhydride, may be mentioned.

PHOSPHINES

1. PRIMARY PHOSPHINES

- MePH₂**. I.^{66, 72, 96} II.⁴ III.⁷ V.⁶⁹ Colorless gas, b. -14° , which liquefies at 0° and 1.75 atmospheres.⁶⁶ Forms crystalline, fairly volatile, salts with HCl and HI.⁶⁶ Very toxic.
- EtPH₂**. I.^{21, 65, 72} III.⁷ V.⁶⁹ VI.¹ B. pt. 25° . Forms crystalline salts with HCl and HI, which are stable only in the concentrated acids. The former yields a chloroplatinate, red solid; the latter is fairly volatile and is best crystallized by addition of ether to the solution of the phosphine in hydriodic acid.⁶⁷
- HOCH₂CH₂PH₂**. VII.⁸⁷ Liquid, b. $139-40^{\circ}$, b_{45} $70-3^{\circ}$, d_4^{20} 1.004, n_D^{20} 1.4950. On treatment with an equivalent amount of sodium, in an inert solvent, followed by acetyl chloride, the O-acetyl derivative is obtained: b_{69} 73° , b_{9-10} $37-8^{\circ}$, d_4^{20} 1.0250, n_D^{20} 1.4620. The O-benzoyl derivative is obtained similarly; b_{20} $142-4^{\circ}$.⁸⁷
- ClCH₂·CO·PH₂**. VIII.¹⁴⁶ Unstable powder.
- Cl₂CH·CO·PH₂**. VIII.⁴² Yellow powder, dec. 200° (from Et₂O-EtOH).⁴²
- Cl₃C·CO·PH₂**. VIII.¹⁶ Crystalline powder.¹⁶
- PrPH₂**. I.¹²⁴ Liquid, b. $53-3.5^{\circ}$.¹²⁴
- Me·CHOH·CH₂FPH₂**. VII. Liquid, b_2 $37-9^{\circ}$, d_4^{20} 0.9764, n_D^{20} 1.4863.⁸⁷
- iso-PrPH₂**. I.⁶⁸ Liquid, b. 41° .
- iso-BuPH₂**. I.⁶⁸ Liquid, b. 62° .
- iso-AmPH₂**. I.⁶⁸ II.⁴ IV.⁵³ Liquid, b. $106-7^{\circ}$.⁶⁸
- n-C₇H₁₅PH₂**. VI. Liquid, b. 169.5° , b_{30} $73-4^{\circ}$.¹⁵⁶ Very readily oxidized.
- n-C₈H₁₇PH₂**. I. Liquid, b. $184-7^{\circ}$, d_4^{17} 0.8209. Salt with HI, crystals, soluble in ether.¹²²
- PhCH₂PH₂**. I.^{67, 92} Liquid, b. 180° , very easily oxidized by air. Forms crystalline salts with HCl and HI.^{67, 92}
- PhPH₂**. IV.^{91, 106, 108} Liquid, b. 160° , d_4^{15} 1.001; sparingly soluble in water or mineral acids. Salt with HI, crystals, m. 138° .
- 4-ClC₆H₄PH₂**. IV.¹⁰⁹ Crystals, m. 17° , b. $198-200^{\circ}$. Chloroplatinate, yellow solid, m. above 270° .¹⁰⁹
- 4-BrC₆H₄PH₂**. IV.¹⁰⁹ Crystals, m. 40° , b. $195-6^{\circ}$.¹⁰⁹
- 4-MeC₆H₄PH₂**. IV.¹¹⁷ Liquid, m. 4° , b. 178° . Salt with HI, needles (from fuming HI); sublimable and unstable in water. Chloroplatinate, yellow crystals.¹¹⁷
- 4-EtC₆H₄PH₂**. IV.¹⁰⁹ Liquid, b. 200° . Salt with HI, crystals, m. 118° . Chloroplatinate, yellow crystals.¹⁰⁹
- 2,4,5-Me₃C₆H₂PH₂**. IV.¹¹⁰ Liquid, b. $214-8^{\circ}$, readily oxidized by air. Chloroplatinate, yellow solid.¹¹⁰
- 2,4,6-Me₃C₆H₂PH₂**. IV.¹¹⁰ Needles, m. 40° , b_{25} 125° . Chloroplatinate, orange needles (from HCl).¹¹⁰
- 4-PhCH₂C₆H₄PH₂**. IV.¹¹¹ Crystals, m. 46° , b_{20} 184° . Salt with HI, needles, m. 134° (from EtOH), unstable in water.¹¹¹
- 4-PhCH₂CH₂C₆H₄PH₂**. IV.¹¹¹ Crystals, m. 75° , b_{45} 190° . Salt with HI, crystals (from conc. HI).¹¹¹

2. SECONDARY PHOSPHINES

- Me₂PH**. I.^{25, 66, 96} Liquid, b. 25° (observed),⁶⁶ b. 21.1° (calc.)²⁵; vapor pressure at -47° is 30 mm.; vapor pressure equation: $\log p = -(1370/T) + 7.539$.²⁵ All salts with mineral acids are soluble; salt with HCl, crystalline, volatile solid; its vapor pressure is 1.3 mm. at 25° and 46 mm. at 75° .¹⁰

- EtP(CN)H.** VIII. Plates, m. 49–50° (from Et₂O); volatile.²³
- MeEtPH.** IV.¹³¹ Low boiling liquid; not isolated in pure state.¹³¹
- Et₂PH.** I.^{65, 72} XVIII.⁹⁶ Liquid, b. 85°. Salts with mineral acids are water-stable; salt with HI, crystals. Chloroplatinate, yellow prisms.^{65, 72}
- (HOCH₂CH₂)₂PH.** VII. Liquid, b. 158–60°, d_4^{20} 1.035, n_D^{20} 1.4892.⁶⁷
- Me(iso-Pr)PH.** IX.⁶⁸ Liquid, b. 78–80°.⁶⁸
- iso-Pr₂PH.** I.⁶⁸ Liquid, b. 118°.⁶⁸
- EtBuPH.** VI.¹⁵³ Liquid, b. 130–50° (impure product).¹⁵³
- Bu₂PH.** IV.¹³¹ VI.¹⁵³ Liquid, b. 169–71°, ¹³¹ b. 180–6(?)°.¹⁵³
- (Me·CHCl·CCl₂·CHOH·)₂PH.** X.⁵⁰ Crystals, m. 96°.⁵⁰
- iso-Pr(iso-Bu)PH.** IX.⁶⁸ Liquid, b. 139–40°.⁶⁸
- iso-Bu₂PH.** I.⁶⁸ Liquid, b. 153°.⁶⁸
- iso-Am₂PH.** I.⁶⁸ Liquid, b. 210–5°.⁶⁸
- MePhPH.** IV. Obtained only in crude state.¹³¹
- EtPhPH.** IV. Obtained only in crude state.¹³¹
- (PhCH₂)₂PH.** I.⁶⁷(?). IX.⁹² Undistillable liquid; ⁹² reported m. 205° is probably that of an oxidation product.⁶⁷
- Ph₂PH.** IV.^{96, 114} XI.³⁹ XVIII.⁹⁶ Liquid, b. 280°, d_4^{16} 1.07. Crystalline salts with HCl and HI are decomposed by water. On being heated with carbon disulfide to 138°, the phosphine forms a product assigned the structure: (Ph₂P·CS₂)H(Ph₂PH), m. 157° (from EtOH).³⁹
- (2-ClC₆H₄)₂PH.** IV.¹³¹ Crystals, m. 67–8°, b. 288–92°.¹³¹
- (4-ClC₆H₄)₂PH.** IV.¹³¹ Crystals, m. 39–40°, b. 314–5°.¹³¹
- (4-O₂N·C₆H₄)₂PH.** IV.¹³¹ Yellow crystals, m. 55–6°, b_{15} 210–20°.¹³¹
- (2-MeC₆H₄)₂PH.** IV.¹³¹ Liquid, b. 306–7°.¹³¹
- Ph(4-MeC₆H₄)PH.** IV.¹³¹ Liquid, b. 286–9°.¹³¹
- (4-MeC₆H₄)₂PH.** IV.¹³¹ Liquid, b. 295–8°.¹³¹
- (1-C₁₀H₇)₂PH.** IV.¹³¹ Crude solid.¹³¹

3. TERTIARY PHOSPHINES

A. COMPOUNDS OF TYPE R₃P

- Me₃P.** IA.^{45, 63} VI.^{13, 149} IX.^{41, 64} XII.¹³⁵ XIII.^{13, 24, 71} XVI.⁴⁰ May be purified through formation of silver iodide complex.^{102, 135} Liquid, b. 37.8°, ¹³⁵ b. 40–2° (impure); ¹³ m. –85.3° to –84.3°.²⁴ Vapor pressure equation: $\log p = -(1518/T) + 7.7627$.¹³⁵ Electron diffraction studies establish a pyramid model, with C-P-C angle of 100° and C-P distance 1.87 Å.¹⁴² The vapor pressure of the salt with HCl is 0.4 mm. at 75° and 14 mm. at 120°.¹⁰ The infrared spectrum has been studied.¹⁵¹
- (ClCH₂)₃P.** XIV.⁵⁷ Liquid, b_7 100°, d_4^{20} 1.414; stable in air.⁵⁷
- Et₃P.** IA.^{45, 63} IB.⁶¹ VI.^{6, 11} XII.^{56, 99} XIII.^{13, 60, 61} (as a by-product, from POCl₃).¹²⁵ XIV.^{17, 93} XIX.⁴¹ Liquid, b. 127°, ⁹⁹ b. 127.5°, d_4^{15} 0.812, $d_4^{18, 6}$ 0.80006, n_D^{18} 1.45799.¹⁶³ Adduct with carbon disulfide, red solid,⁶¹ m. 121–2° (from EtOH),¹⁵⁹ m. 95°, ⁵⁵ yields a methiodide, m. 96–7°.⁵⁵ The phosphine forms an adduct with *p*-benzoquinone (black solid, m. 180°),³⁶ and with iodobenzene (rather unusual).¹³⁹ The carbon disulfide adduct adds hydrogen chloride, yielding an acid-stable product: Et₃P(Cl)CS₂H,⁶¹ which decomposes in water, forming sulfur and hydrogen sulfide. On heating with aqueous hydrogen sulfide, the adduct forms a yellow solid, C₈H₁₇S₃P (besides Et₃PS), which on treatment with water forms an -onium compound, C₇H₁₈SPOH, which forms a crystalline iodide, which, in turn, yields MeEt₃POH, on treatment with silver oxide.⁶² Double salts with AuCl,^{12, 94} needles,

dec. 80°; with CuI ,³ plates, m. 37–9° (from ligroin); with ZnI_2 ($2\text{Et}_3\text{P} \cdot \text{ZnI}_2 \cdot 2\text{HI}$),^{11, 61} crystals (from water); with PdCl_2 ,¹² yellow prisms (from EtOH or Et_2O); with PtCl_2 , two forms—soluble and insoluble in ether, apparently *cis* and *trans* forms;^{12, 37, 86, 141, 158} with PtCl_4 ,¹³ crystals (from water).

(HOCH₂CH₂)₃P. VII.⁸⁷ Liquid, b. 183–5°, d_4^{20} 1.053, n_D^{20} 1.4780.⁸⁷

Pr₃P. XII.^{35, 44, 99} Liquid, b_{50} 103.5°, ³⁵ b. 187.5°, ³⁵ b_{24} 85.5–87°, ⁹⁹ b_{16} 17 121–2(?)°, b_{12} 72–3°, ⁴⁴ d_4^{25} 0.807.³⁵ CS_2 adduct, m. 108°. ³⁵ Salt with HgCl_2 , m. 137°. ³⁵

(Me·CHOH·CH₂)₃P. VII. Liquid, b_5 65°, d_4^{20} 1.035, n_D^{20} 1.4620.⁸⁷

(CH₂:CH·CH₂)₃P. XII.⁸³ Liquid, b_{13} 69°. HgCl_2 salt, m. 135° (from EtOH). Adduct with CS_2 , red needles, m. 32.5°; adduct with *p*-benzoquinone, yellow, dec. 100° (from $\text{EtOH-Et}_2\text{O}$).⁸³

(Me(HO₂C)C(OH))₃P. Isolated only as an anhydride, $(\text{Me}(\text{O}_2\text{C})\text{C})_3\text{P} : \text{XA}$.¹⁰⁴ Needles, unstable in aqueous acid solutions.¹⁰⁴

(iso-Pr)₃P. IX.⁶⁸ XII.²⁶ Liquid, b_{22} 81°. ²⁶ Salt with HI , crystals.⁶⁸ CS_2 adduct, m. 111°. ²⁶

Bu₃P. XII.^{30, 44, 99} Liquid, b_{50} 149.5°, ³⁰ b_{32} 136–7°, b_{22} 129–30°, ⁹⁹ b_{16} 121–2°, ⁴⁴ d_4^{25} 0.8118.³⁰ Adduct with *p*-benzoquinone, yellowish, m. 180–90°. ³⁶ Adduct with CS_2 , red, m. 65.5°. ³⁰

iso-Bu₃P. IX.⁶⁸ XII.³⁵ Liquid, b. 215°, ⁶⁸ b_{50} 126°. ³⁵ HgCl_2 salt, m. 191.5°. ³⁵

(CH₂:CMe·CH₂)₃P. XII. Liquid, b_{15} 112°. Adduct with HgCl_2 , plates, m. 162°; adduct with *p*-benzoquinone, dec. 200°. Very easily oxidized by exposure to air.⁸³

Am₃P. XII.^{35, 99} Solid (when pure), m. 29°, ⁹⁹ b_{50} 185.5°, ³⁵ b_{19} 165–6°. ⁹⁹ Its adduct with CS_2 is a red solid, m. 55°. ³⁵

(MeEtCH)₃P. XII (very poor yield).²⁶ Liquid, b_{11} 108°. CS_2 adduct, m. 66°. ²⁶

(MeEtCH·CH₂)₃P. XII. Liquid, b_{10} 113–7°. ³⁵

iso-Am₃P. XII.^{35, 143} Liquid, b_{11} 131°, ³⁵ b_{11} 131–2°. ¹⁴³ CS_2 adduct, red, m. 79.5°.

(C₆H₁₃)₃P. XII. Crystals, m. 20°, b_{50} 227°. ⁷⁷

(C₇H₁₅)₃P. XII. Crystals, m. 20°, b_{50} 260°, d_4^{25} 0.833.⁷⁷

(C₈H₁₇)₃P. XII. Crystals, m. 30°, b_{50} 291°. ⁷⁷

(PhCH₂)₃P. I. IX. Crystals with very high boiling point.⁹²

Ph₃P. XII.^{38, 98, 99, 127} XV.^{114, 118, 120} XX.^{90, 147} Prisms, m. 79° (from $\text{EtOH-Et}_2\text{O}$), b. 360° (dec.), b_1 188°. ¹⁵² Feebly basic and easily precipitated from solution in fuming hydrochloric acid by dilution; HI salt, m. 215°, is decomposed by water. Does not form an adduct with carbon disulfide, but forms double salts with HgCl_2 (needles, m. above 300°), ^{89, 120} with PtCl_4 (yellow solid), with SbCl_3 (solid, m. 96°), with AsCl_3 (solid, m. 100°), and with BiCl_3 (solid, m. 100–5°).¹⁴ Adduct with *p*-benzoquinone, crystals, m. 253°. ¹⁴⁰

(2-ClC₆H₄)₃P. XII. Crystals, m. 185° (from EtOH).⁹⁸

(3-ClC₆H₄)₃P. XII. Crystals, m. 67°. ⁹⁸

(4-ClC₆H₄)₃P. XII. Crystals, m. 103° (from EtOH).⁹⁸

(2-MeOC₆H₄)₃P. XII. Crystals, m. 204° (from EtOH).⁹⁸

(3-MeOC₆H₄)₃P. XII. Crystals, m. 115° (from EtOH).⁹⁸

(4-MeOC₆H₄)₃P. XII. Crystals, m. 131° (from EtOH).⁹⁸

(4-PhOC₆H₄)₃P. XII (best, from RPCl_2). Crystals, m. 111° (from benzene- EtOH).³³

(4-Me₂NC₆H₄)₃P. XVII.^{9, 54, 88, 119, 138} Needles (from dil. EtOH), m. 275°, ¹³⁸ m. 273°, ¹¹⁹ m. 308°(?), ⁸⁸ develops blue color on air exposure, caused by traces of crystal violet.⁸⁸ Soluble in dil. HCl .¹¹⁹

(4-Et₂NC₆H₄)₃P. XVII.⁸³ Needles, m. 274° (from EtOH).

(2-MeC₆H₄)₃P. XII. Crystals, m. 125° (from EtOH).⁹⁸

- (3-MeC₆H₄)₃P. XII. Crystals, m. 100° (from EtOH).⁹⁸
 (4-MeC₆H₄)₃P. XII.⁹⁸ XV.¹¹¹ Prisms, m. 146° (from EtOH).^{98,111}
 (2,4-Me₂C₆H₃)₃P. XV. Needles, m. 154° (from EtOH). HgCl₂ salt, dec. 270°.¹¹¹
 (2,5-Me₂C₆H₃)₃P. XV. Needles, m. 155° (from AcOH). HgCl₂ salt, m. 256°.¹¹¹
 (2,4,5-Me₃C₆H₂)₃P. XV. Needles (from CHCl₃-ligroin), m. 216-7°.¹¹¹
 (2,4,6-Me₃C₆H₂)₃P. XV. Powder, m. 205-6°; forms crystalline HgCl₂ salt.¹¹¹
 (1-C₁₀H₇)₃P. XII.¹³¹ Plates, m. 189-90° (from benzene-Et₂O),¹³¹ m. 282°(?) (from dioxan).² Adduct with chloroform, m. 262°.²
 (2-PhC₆H₄)₃P. XV (using a little antimony metal catalyst).¹⁶² Plates, m. 151-2° (from EtOH).¹⁶²
 (4-PhC₆H₄)₃P. XV (as above).¹⁶¹ Needles, m. 172° (from benzene). Displays not a trace of disproportionation with PCl₃ at 250°.¹⁶¹
Tri-(2-pyridyl)phosphine. XII.^{32,101} Crystals, m. 115°,¹⁰¹ m. 113-4° (from MeOH).³² b_{0,15} 210°.³² Trihydrochloride, m. 207.5-9.5°;¹⁰¹ dipicrate, m. 142-3°.¹⁰¹
Tri-(3-indolyl)phosphine. XII. Crystals, m. 195-6° (from Me₂CO-EtOH).¹²¹ Stable to hot aqueous alkali; forms an N-silver derivative with ammoniacal silver nitrate. Separable from the (N)-P analog by solubility in acetone.¹²¹
Tri-(3-methyl-2-indolyl)phosphine. XII. Crystals, m. 156-8° (from ligroin).¹²¹ Similar to the previous compound.

B. COMPOUNDS OF TYPE R₂R'P

- Me₂EtP. XIV. Liquid, b. 83-5°. Salt with PtCl₄, crystals.¹⁸
 Me₂(PhCH₂)P. XII. Liquid, b₁₂ 93-6°.⁸⁰
 Me₂PhP. XII.^{98,103} XIII.¹⁰⁸ Liquid, b. 192°,¹⁰⁸ b. 190°,¹⁰⁸ b_{13,5} 83-4°,¹⁰³ b₂₀ 82°,⁹⁸ d₄¹¹ 0.9678.¹⁰⁸ Monohydrochloride is a solid; dihydrochloride is a liquid. Salt with PtCl₄, m. 160°.^{108,115} CS₂ adduct, red solid, m. 97° (in open tube),²² m. 102° (in sealed tube).³⁶ Heating the phosphine with benzal chloride, with treatment of the product with water, or heating with benzaldehyde (AlCl₃ catalyst used) yields a quaternary compound, probably Ph·CHOH·PPh(Me₂)(Cl), which forms a chloroplatinate, m. 50°.⁷³
 Me₂(4-MeOC₆H₄)P. XII. CS₂ adduct, m. 119°.³⁶
 Me₂(4-PhOC₆H₄)P. XII. Liquid, b₁₃ 183°,²⁰ d₄²⁰ 1.1037.³³ CS₂ adduct, m. 88°,³⁶ m. 87.5°.³⁴
 Me₂(4-BrC₆H₄)P. XII. Liquid, b_{17,5} 99°,²² b₄ 55°. CS₂ adduct, m. 96°.³⁶
 Me₂(4-Me₂NC₆H₄)P. XIII. Liquid, b. 265°. CS₂ adduct, m. 162°.¹¹⁹
 Me₂(4-MeC₆H₄)P. XII.^{36,98} XIII.²² Liquid, b. 210°,²² b₁₂ 93-5°.⁹⁸ CS₂ adduct, red plates, m. 110° (open tube),²² m. 118° (sealed tube).³⁶ Adduct with *p*-benzoquinone, cream-colored solid, m. above 250°.³⁶
 Me₂(4-PhCH₂C₆H₄)P. XIII. Liquid, b₂₀ 197°.¹¹¹
 Me₂(4-PhCH₂CH₂C₆H₄)P. XIII. High boiling liquid.¹¹¹
 Me₂(3,4-Me₂C₆H₄)P(?). XIII.^{20,22} Liquid, b. 230°,²² b. 233°.²⁰ The precise structure of this phosphine is in doubt. CS₂ adduct, red plates, m. 115°.²²
 Me₂(2,5-Me₂C₆H₃)P. XII.^{36,78} XIII.²² Liquid, b₁₂ 106°,²² d₄²⁵ 0.9541.⁷⁸ CS₂ adduct, red plates, m. 76°,⁷⁸ m. 72° (sealed tube).³⁶ Double salt with HgCl₂, m. 225°.²²
 Me₂(2,4,6-Me₃C₆H₂)P. XII.^{27,36} Liquid, b₁₆ 133°,²⁷ b₆ 100°,³⁶ d₄²⁵ 0.9570,²⁷ n_D²⁵ 1.5554.²⁷ CS₂ adduct, red solid, m. 58-9°,²⁷ m. 46° (sealed tube).³⁶
 Et₂MeP. XIV.¹⁸ Liquid, b. 110-2°.¹⁸
 Et₂PrP. XIV. Liquid, b. 146-9°.¹⁸
 Et₂(iso-Am)P. XIV. Liquid, b. 185-7°. Hydrochloride is volatile at 270°.¹⁸
 Et₂(PhCH₂)P. XIV. Liquid, b. 250-5°.¹⁸ Hydrochloride is volatile at 325°. An apparently crude product has been reported: VI. Liquid, b. 240-60°.¹⁵³

- Et₂PhP.** XII.^{84, 98, 108} XIII.^{108, 112} Liquid, b. 221.9°, ¹⁰⁸b₂₉ 120–1°, ⁸¹b₂₀ 108–9°, ⁹⁴b₁₀ 96–8°, ¹⁰³b₁₀ 96–7°, ⁸⁴d₄¹³ 0.9571, ⁹⁸d₄²⁰ 0.9545, ²⁰n_D²⁰ 1.5458, ⁸¹ Mono- and dihydrochlorides have been isolated,¹⁰⁸ yielding a salt with PtCl₄, yellow crystals.^{108, 112} CS₂ adduct, red solid,²² m. 45°. ⁸⁶
- Et₂(4-HOC₆H₄)P.** By treatment of the 4-methoxy derivative with hydriodic acid at 135° in inert atmosphere. Liquid, b₁₉ 168–76°. It is best purified as the methiodide, m. 168–9°. ⁸²
- Et₂(4-MeOC₆H₄)P.** XII.^{31, 32, 36} XIII.¹⁰⁹ Liquid, b. 266–7°, ¹⁰⁹b₄₀ 166–71°, ⁸²b₁₀ 130–1°, ⁸¹d₀¹⁸ 0.9978, ¹⁰⁹d₄²⁰ 1.0015, ²⁰n_D²⁰ 1.5498, ⁸¹ Platinichloride, m. 103°. ¹⁰⁹
- Et₂(4-EtOC₆H₄)P.** XIII.¹⁰⁹ Liquid, b. 275°. ¹⁰⁹
- Et₂(4-PhOC₆H₄)P.** XII. Liquid, b₁₃ 208°, ⁸³b₁₀ 199–200°, ⁸¹d₄²⁰ 1.0743, ⁸¹d₄²⁰ 1.0711, ⁸³n_D²⁰ 1.5968, ⁸¹ CS₂ adduct, m. 69°, ⁸⁶m. 67°. ⁸⁴
- Et₂(4-Me₂NC₆H₄)P.** XII.³⁶ XIII.¹¹⁹ Liquid, m. 12.5°, b. 298°. ¹¹⁹ CS₂ adduct, m. 107°, ¹¹⁹m. 103°. ³⁶
- Et₂(4-ClC₆H₄)P.** XIII.¹⁰⁹ XII.⁸¹ Liquid, b. 255–7°, ¹⁰⁹b₁₅ 129–30°, ⁸¹d₄²⁰ 1.0708, ²⁰n_D²⁰ 1.5603. ⁸¹
- Et₂(4-BrC₆H₄)P.** XII.⁸¹ XIII.¹⁰⁹ Liquid, b. 265°, ¹⁰⁹b₁₅ 141–3°, ⁸¹d₄²⁰ 1.2886, ²⁰n_D²⁰ 1.5821. ⁸¹ CS₂ adduct, very unstable solid. ⁸⁶
- Et₂(2-MeC₆H₄)P.** XIII. Liquid, b. 263°. ¹⁰⁹
- Et₂(4-MeC₆H₄)P.** XII.^{31, 98} XIII.²² Liquid, b. 240°, ²²b₁₃ 113.5–4.5°, ⁸¹b₁₂ 114–5°, ⁹⁸d₄²⁰ 0.9373, ²⁰n_D²⁰ 1.5428, ⁸¹ CS₂ adduct, m. 55° (sealed tube). ⁸⁶
- Et₂(4-EtC₆H₄)P.** XIII. Liquid, b. 268–70°, ²⁵d₀⁵ 0.929. ¹⁰⁹ Solution in hydrochloric acid yields a chloroplatinate, yellow crystals. ¹⁰⁹
- Et₂(4-PhCH₂C₆H₄)P.** XIII. Liquid, b₂₀ 235°. ¹¹¹
- Et₂(4-PhCH₂CH₂C₆H₄)P.** XIII. High boiling liquid. ¹¹¹
- Et₂(2,5-Me₂C₆H₃)P.** XII.⁷⁸ XIII.²² Liquid, b. 260°, ²²b₅₂ 157°, ²⁵d₄²⁵ 0.9392. Double salt with HgCl₂, needles, m. 184°; ⁷⁸with HgI₂, solid, m. 105°.
- Et₂(2,5- or 5,2-Me(iso-Pr)C₆H₃)P.** XIII. Liquid, b. 260–70°. ¹¹⁰
- Et₂(2,4,5-Me₃C₆H₂)P.** XIII. Liquid, b. 274–5°. Chloroplatinate, red. ¹¹⁰
- Et₂(2,4,6-Me₃C₆H₂)P.** XIII. Liquid, b. 270°. Chloroplatinate, orange. ¹¹⁰
- Et₂(1-C₁₀H₇)P.** XIII. Yellow liquid, b. 360° (dec.). ⁸⁵
- Diethyl-2-thienylphosphine.** XIII. Liquid, b. 225°. ¹³⁶
- (EtO₂C)₂PhP.** XIXA (by treatment of phenylphosphine with phenylmagnesium bromide, followed by reaction with ethyl chlorocarbonate). Liquid, b₄₋₆ 150–3°. ⁸¹
- Pr₂PhP.** XII. Liquid, b₅₀ 159°, ²⁵d₄²⁵ 0.925. Double salt with HgCl₂, m. 192.5° (from EtOH). ³⁵
- Pr₂(4-MeOC₆H₄)P.** XII. Liquid, b₁₇ 165°, ²⁵d₄²⁵ 0.9738, ²⁵n_C²⁵ 1.5301, ²⁵n_D²⁵ 1.5352, ²⁵n_F²⁵ 1.5477. ⁷⁶ Double salt with HgCl₂, m. 134°. ⁷⁶
- Pr₂(4-PhOC₆H₄)P.** XII. Liquid, b₁₃ 218°. ³³ CS₂ adduct, m. 57°. ⁸⁴
- Pr₂(4-MeC₆H₄)P.** XII. Liquid, b₅₀ 174°, ²⁵d₄²⁵ 0.921. ⁸⁵ HgCl₂ salt, m. 129.5°. ⁸⁵
- Pr₂(4-EtC₆H₄)P.** XII. Liquid, b₂₁ 157°, ²⁵d₄²⁵ 0.9147, ²⁵n_C²⁵ 1.5208, ²⁵n_D²⁵ 1.5255, ²⁵n_F²⁵ 1.5370. ⁷⁸
- Pr₂(2,5-Me₂C₆H₃)P.** XII. Liquid, b₂₅ 161°, ²⁵d₄²⁵ 0.9281. ⁷⁸ HgCl₂ salt, needles, m. 188°. ⁷⁸
- (CH₂:CH·CH₂)₂PhP.** XII. Liquid, b₁₄ 127°, ²⁵d₄²⁵ 0.9693, ²⁵n_D²⁵ 1.5670. Salt with HgCl₂, needles, m. 123°. ⁸³
- (CH₂:CH·CH₂)₂(4-BrC₆H₄)P.** XII. Liquid, b₃₇ 186°, ²⁵d₄²⁵ 1.2783, ²⁵n_D²⁵ (unreported). Salt with HgCl₂, needles, m. 108°. ⁸³
- (CH₂:CH·CH₂)₂(4-MeOC₆H₄)P.** XII. Liquid, b₁₅ 162°, ²⁵d₄²⁵ 1.0189, ²⁵n_D²⁵ 1.5705. Salt with HgCl₂, prisms, m. 131°. ⁸³

- (CH₂:CH·CH₂)₂(4-PhOC₆H₄)P.** XII. Liquid, *b*₁₆ 238°, *d*₄²⁵ 1.0847, *n*_D²⁵ 1.6040. Salt with HgCl₂, solid, dec. 210°. ⁸³
- (CH₂:CH·CH₂)₂(4-MeC₆H₄)P.** XII. Liquid, *b*₁₄ 138°, *d*₄²⁵ 0.9651, *n*_D²⁵ 1.5545. Salt with HgCl₂, prisms, m. 110.5°. ⁸³
- (CH₂:CH·CH₂)₂(4-EtC₆H₄)P.** XII. Liquid, *b*₁₀ 145°, *d*₄²⁵ 0.9484, *n*_D²⁵ 1.5545. ⁸⁸
- (CH₂:CH·CH₂)₂(4-iso-PrC₆H₄)P.** XII. Liquid, *b*₁₁ 153°, *d*₄²⁵ 0.9361, *n*_D²⁵ 1.5435. Salt with HgCl₂, crystals, m. 47°. ⁸³
- (CH₂:CH·CH₂)₂(2,5-Me₂C₆H₃)P.** XII. Liquid, *b*₁₃ 144°, *d*₄²⁵ 0.9584, *n*_D²⁵ 1.5540. Salt with HgCl₂, rhombic crystals, m. 170°. ⁸³
- iso-Pr₂(4-PhOC₆H₄)P.** XII. Liquid, *b*₁₈ 209°, *d*₄²⁵ 1.0423, *n*_D²⁵ 1.5826. ⁸⁶
- Bu₃PhP.** XII. Liquid, *b*₅₀ 184.5–5.5°, *d*₄²⁵ 0.9115. Salt with HgCl₂, needles, m. 160.5°. ⁸⁰
- Bu₂(4-MeOC₆H₄)P.** XII. Liquid, *b*₁₆ 190°, *d*₄²⁵ 0.9600, *n*_C²⁵ 1.5226, *n*_D²⁵ 1.5274, *n*_F²⁵ 1.5389. ⁷⁶
- Bu₂(4-PhOC₆H₄)P.** XII. Liquid, *b*₁₃ 235°, *d*₄²⁰ 1.0310. ⁸³
- Bu₂(4-MeC₆H₄)P.** XII. Liquid, *b*₅₀ 197°, *d*₄²⁵ 0.9076. Salt with HgCl₂, prisms, m. 112° (from EtOH). ⁸⁰
- Bu₂(4-EtC₆H₄)P.** XII. Liquid, *b*₁₅ 176°, *d*₄²⁵ 0.9042, *n*_C²⁵ 1.5162, *n*_D²⁵ 1.5208, *n*_F²⁵ 1.5319. ⁷⁶
- Bu₂(2,5-Me₂C₆H₃)P.** XII. Liquid, *b*₁₆ 171°, *d*₄²⁵ 0.9124. Salt with HgCl₂, needles, m. 179°. ⁷⁸
- iso-Bu₂PhP.** XII. Liquid, *b*₅₀ 168°, *d*₄²⁵ 0.910. Salt with HgCl₂, needles, m. 158.5°. ⁸⁵
- iso-Bu₂(4-MeC₆H₄)P.** XII. Liquid, *b*₅₀ 182.5–4.5°, *d*₄²⁵ 0.915. ⁸⁵
- iso-Bu₂(2,5-Me₂C₆H₃)P.** XII. Liquid, *b*₂₀ 184°. Salt with HgCl₂, m. 227°. ⁷⁸
- (CH₂:CMe·CH₂)₂PhP.** XII. Liquid, *b*₁₈ 148°, *d*₄²⁵ 0.9484, *n*_D²⁵ 1.5485. Salt with HgCl₂, plates, m. 140.5°. ⁸³
- (CH₂:CMe·CH₂)₂(4-BrC₆H₄)P.** XII. Liquid, *b*₁₈ 189°, *d*₄²⁵ 1.2094, *n*_D²⁵ 1.5752. Salt with HgCl₂, cubes, m. 194°. ⁸³
- (CH₂:CMe·CH₂)₂(4-MeOC₆H₄)P.** XII. Liquid, *b*₂₀ 192°, *d*₄²⁵ 0.9948, *n*_D²⁵ 1.5513. Salt with HgCl₂, cubes, m. 181°. ⁸³
- (CH₂:CMe·CH₂)₂(4-MeC₆H₄)P.** XII. Liquid, *b*₂₃ 168°, *d*₄²⁵ 0.9426, *n*_D²⁵ 1.5465. Salt with HgCl₂, cubes, m. 164°. ⁸³
- (CH₂:CMe·CH₂)₂(4-EtC₆H₄)P.** XII. Liquid, *b*₂₀ 178°, *d*₄²⁵ 0.9360, *n*_D²⁵ 1.5435. Salt with HgCl₂, prisms, m. 156°. ⁸³
- (CH₂:CMe·CH₂)₂(4-iso-PrC₆H₄)P.** XII. Liquid, *b*₁₉ 182.5°, *d*₄²⁵ 0.9279, *n*_D²⁵ 1.5350. Salt with HgCl₂, needles, m. 153°. ⁸³
- (CH₂:CMe·CH₂)₂(2,5-Me₂C₆H₃)P.** XII. Liquid, *b*₁₆ 166°, *d*₄²⁵ 0.9402, *n*_D²⁵ 1.5450. Salt with HgCl₂, prisms, m. 201–2°. ⁸³
- Am₂PhP.** XII. Liquid, *b*₅₀ 210°, *d*₄²⁵ 0.902. Salt with HgCl₂, m. 108°. ⁸⁵
- Am₂(4-MeOC₆H₄)P.** XII. Liquid, *b*₁₈ 202°, *d*₄²⁵ 0.9382, *n*_C²⁵ 1.5132, *n*_D²⁵ 1.5178, *n*_F²⁵ 1.5289. Salt with HgCl₂, m. 114° (from AcOH). ⁷⁶
- Am₂(4-MeC₆H₄)P.** XII. Liquid, *b*₅₀ 220°, *d*₄²⁵ 0.898. Salt with HgCl₂, m. 112° (from AcOH). ⁸⁵
- Am₂(4-EtC₆H₄)P.** XII. Liquid, *b*₁₈ 201°, *d*₄²⁵ 0.9022. Salt with HgCl₂, m. 95° (from AcOH). ⁷⁶
- Am₂(2,5-Me₂C₆H₃)P.** XII. Liquid, *b*₂₃ 214°. Salt with HgCl₂, cubes, m. 117°. ⁷⁸
- (MeEtCH·CH₂)₂PhP.** XII. Liquid, *b*₅₀ 198°, *d*₄²⁵ 0.906. Salt with HgCl₂, m. 120°. ⁸⁴
- (MeEtCH·CH₂)₂(4-MeC₆H₄)P.** XII. Liquid, *b*₅₀ 210–1°, *d*₄²⁵ 0.902. Salt with HgCl₂, m. 99°. ⁸⁵

- iso-Am₂PhP.** XII. Liquid, b_{50} 198.5°, d_4^{25} 0.900. Salt with HgCl₂, m. 152°. ³⁵
- iso-Am₂(4-MeC₆H₄)P.** XII. Liquid, b_{50} 210°, d_4^{25} 0.824. Salt with HgCl₂, m. 107° (from AcOH). ³⁵
- (C₆H₁₃)₂PhP.** XII. Liquid, b_{50} 236°, d_4^{20} 0.901. ⁷⁷
- (Me₂CH·CH₂CH₂CH₂)₂PhP.** XII. Liquid, b_{50} 219°. ³⁶
- (Me₂CH·CH₂CH₂CH₂)₂(4-MeC₆H₄)P.** XII. Liquid, b_{50} 234–5°, d_4^{25} 0.888. Salt with HgCl₂, m. 110.5° (from AcOH). ³⁵
- (C₇H₁₅)₂PhP.** XII. Liquid, b_{50} 260°, d_4^{20} 0.895. ⁷⁷
- (C₈H₁₇)₂PhP.** XII. Liquid, b_{50} 277°, d_4^{20} 0.890. ⁷⁷
- (PhCH₂)₂EtP.** XIV (from Et₂(PhCH₂)₂PCl). Liquid, b. 320–30°. ¹⁸
- (PhCH₂)₂PhP.** XIV (by-product; from Et₂Ph(PhCH₂)PCl). Liquid, b_{10} 170°. ⁸⁴
- An attempt to prepare this phosphine, by modified XIII, resulted in a substance, C₁₃H₁₃P, m. 169–70°, which did not possess the expected phosphine-like properties. ¹¹⁴
- Ph₂MeP.** XIII. Liquid, b. 284°, d_4^{15} 1.0784. ¹¹⁵
- Ph₂EtP.** XIII. ¹¹⁶ XII. ¹⁰³ Liquid, b. 293°, ¹¹⁶ b_{22} 184°. ¹⁰³
- Ph₂(4-ClC₆H₄)P.** XV. Liquid. ¹¹¹
- Ph₂(4-BrC₆H₄)P.** XII. Liquid, b_4 205–10°. ⁴⁷
- Ph₂(4-MeOC₆H₄)P.** XV. Liquid. ¹¹¹
- Ph₂(4-Me₂NC₆H₄)P.** XV. Crystals, m. 152° (from Et₂O-EtOH), soluble in 1:1 hydrochloric acid, precipitated on dilution. ¹¹⁹
- Ph₂(4-MeC₆H₄)P.** XV. Prisms, m. 68°, soluble in concentrated hydrochloric acid, precipitated by dilution. ³⁹
- Ph₂(EtO₂C)P.** XIXA. Liquid, b_{5-6} 185–6°. ⁸¹
- Ph₂(4-HO₂CC₆H₄)P.** By treatment of the 4-bromo analog with butyl-lithium, followed by treatment with carbon dioxide. Crystals, m. 156° (from AcOH). ⁴⁷
- Ph₂(3-HO₂CC₆H₄)P.** By treatment of triphenylphosphine with butyl-lithium, followed by treatment with carbon dioxide. Also obtained by the reaction of diphenylchlorophosphine with *m*-bromophenylmagnesium bromide, followed by treatment of the product with butyl-lithium and carbon dioxide. Crystals, m. 157° (from EtOH). ⁴⁷
- Ph₂(2-C₆H₄N)P.** XII. Crystals, m. 84–5° (from dil. MeOH), $b_{0.05}$ 132–80° (crude). Picrate, m. 137–8° (from Me₂CO-EtOH). ¹⁰¹
- (4-H₂NC₆H₄)₂PhP.** From phenyldichlorophosphine and *p*-aminophenyl-lithium in ether. Undistillable oil. Diacetyl derivative, m. 169° (from 50% EtOH). Di-(*p*-acetylaminobenzenesulfonyl) derivative, m. 186–7° (from 30% EtOH). Di-(*p*-aminobenzenesulfonyl) derivative, by hydrolysis of the above compound with hot dilute sodium hydroxide, m. 202–4° (from EtOH). ⁴⁸
- (4-MeC₆H₄)₂MeP.** XIII. Liquid, b. 345°. ¹¹¹
- (4-MeC₆H₄)₂(PhCH₂)P.** XV. Needles, m. 187°(?). ¹¹¹
- (4-MeC₆H₄)₂PhP.** XV. Crystals, m. 57°. ³⁹
- (4-MeC₆H₄)₂(4-MeOC₆H₄)P.** XV. Liquid. ¹¹¹
- (4-MeC₆H₄)₂(4-ClC₆H₄)P.** XV. Crystals, m. 115° (from ligroin). ¹¹¹
- (2-C₆H₄N)₂PhP.** XII. Crystals, m. 96° (from EtOH-ligroin), $b_{0.4}$ 196–210° (crude). Dihydrochloride, m. 185–7°; dipicrate, m. 131°. ¹⁰¹

C. (P)-CYCLIC DERIVATIVES

- (CH₂CH₂)₂PPh.** XII. Liquid, b_{16-18} 132–3°, d_4^0 1.0502, d_4^{10} 1.0429, d_4^{20} 1.0354, d_4^{30} 1.0281, n_D^{25} 1.5894. Salt with HgCl₂, m. 143–4° (from benzene). ⁵²
- CH₂(CH₂CH₂)₂PPh.** XII. Liquid, b_{22-4} 154–5°, b_{16-18} 143–4°, d_4^{21} 1.0306, n_D^{20} 1.5886. Salt with HgCl₂, dec. 172°. ⁵²

O(CH₂CH₂)₂PPh. XIXA. Crystals, m. 135–7° (from EtOH).⁹¹

CH₂(CH₂CH₂)₂PC₆H₄Me-4. XII. Liquid, b₂₄ 167–8°, d₄²⁰ 1.0007, n_D²² 1.5729. Salt with HgCl₂, needles, m. 157°.⁶²

4-MeC₆H₄PCH₂CH₂C₆H₄CH₂-(1,2). XV. Oil, b_{0.1} 150–80°.⁷⁴

D. COMPOUNDS OF TYPE RR'R''P

Et(iso-Pr)(iso-Bu)P. IX. Liquid, b. 190°.⁶⁸

MePh(4-MeC₆H₄)P. XII. Undescribed.¹³²

EtPh(PhCH₂)P. XIV (from Et₂Ph(PhCH₂)P)⁺,^{84,103} among by-products. Liquid, b₃₃ 204–6°,¹⁰³ b₁₀ 156–60°.⁸⁴

EtPh(4-BrC₆H₄)P. XII. Liquid, b_{0.05} 136–8°. Salt with PdCl₂, orange crystals, m. 172.5–74°.³²

EtPh(4-HOC₆H₄)P. By treatment of the 4-methoxy analog with hot hydriodic acid (125–30°) in inert atmosphere. Oil, b_{0.1} 160–75°; benzoyl derivative, m. 79–80° (from EtOH).³²

EtPh(4-MeOC₆H₄)P. XII. Liquid, b_{0.1} 137°, b₂₀ 210–1°.³²

EtPh(4-MeC₆H₄)P. XII.¹⁵⁷ XIII.¹¹¹ Liquid, b. 340°.¹¹¹

EtPh(2,4,5-Me₃C₆H₂)P. XIII. Liquid, b. 352°, b₁₀ 225–30°. Yields crystalline salts with HgCl₂ and PtCl₄.¹¹¹

PrPh(4-MeOC₆H₄)P. XII. Liquid, b_{0.3} 163.5°.³²

BuPh(4-MeOC₆H₄)P. XII. Liquid, b_{0.025} 139–41°, b_{0.5} 176–9°.³²

BuPh(4-HOC₆H₄)P. Could not be isolated after refluxing the above substance with hydriodic acid in inert atmosphere, followed by neutralization. However, conversion into the benzoate (by using benzoyl chloride) gave the benzoate in a pure state, m. 91° (from EtOH).³²

Ph(4-BrC₆H₄)(2-MeOCH₂C₆H₄CH₂CH₂)P. XII. Green oil, b_{0.1} 214–6°.⁷⁴

Ph(4-MeOC₆H₄)(2-MeOCH₂C₆H₄CH₂CH₂)P. XII. Liquid, b_{0.05} 208°.⁷⁴

Ph(4-BrC₆H₄)(4-MeOC₆H₄)P. XII. Crystals, m. 71° (from MeOH), b_{0.01} 204°.³²

Ph(4-BrC₆H₄)(4-Me₂NC₆H₄)P. XII (somewhat better yield is obtained by using organolithium compound, rather than RMgX). Crystals, m. 107–8° (from EtOH), b_{0.05} 218–20°.³² Salt with PdCl₂, orange solid, dec. 247–9°.³²

Ph(4-MeOC₆H₄)(4-MeC₆H₄)P. XII. Crystals, m. 116–8° (from MeOH), b_{0.1} 197–200°, b_{0.03} 176–83°.³²

Ph(4-BrC₆H₄)(2-C₆H₄N)P. XII. Crystals, m. 90–1° (from MeOH), b_{0.01} 180–230° (crude). Picrate, m. 132° (from EtOH).³²

Ph(4-BrC₆H₄)(3-C₆H₄N)P. XII. Oil, b_{0.15} 202–10°; picrate, m. 143–4°.³²

BIPHOSPHINES AND RELATED PRODUCTS

Ph₂P·PPh₂. By heating diphenylchlorophosphine with diphenylphosphine.⁸⁹ By thermal decomposition of phosphobenzene, PhP:PPh(?).¹¹⁵ Crystals, m. 67°, b. above 400°.

PhP:PPh(?). By reaction of phenyldichlorophosphine with phenylphosphine in inert atmosphere.¹¹⁵ Yellow powder, m. 149–50°. Chlorination yields phenyldichlorophosphine, while hydrogen chloride regenerates the starting materials: phenyldichlorophosphine and phenylphosphine(?).¹¹⁵

PhAs:PPh. By reaction of phenylarsine with phenyldichlorophosphine. Yellow needles, m. 181°. Poorly stable to heat;¹⁴⁸ on heating dissociates into PhAs:AsPh and PhP:PPh.¹⁴⁸

- PhP:POH(?)**. By reaction of diphosphine (P_2H_4) with phenyldichlorophosphine, followed by treatment with alcohol. Yellow powder, which on oxidation yields benzenephosphonic acid. The individuality of the product may be in some doubt.¹⁰⁷
- PhP₄H·(?)**. By treatment of phenyldichlorophosphine with one mole of water with heating. Yellow, easily oxidizable solid, formed among many poorly defined products, which yield benzenephosphonic acid on oxidation.¹⁰⁷
- Me₂P·PMe₂(?)**. Reported as one of the products resulting from the passage of methyl chloride over heated calcium phosphide.¹⁴⁹ Also reported as a by-product from the reaction of methyl iodide with sodium phosphide.¹³ Liquid, b. 250°, easily oxidized by air to dimethylphosphonic acid.¹³

PHOSPHINEMETHYLENES

- Ph₃P:CPh₂**. By decomposition of $Ph_3P:N_2:CPh_2$ at 185° in vacuo. Red plates, m. 170–2°; reacts with moisture.¹⁴⁶ The product is prepared more conveniently from butyl-lithium and triphenylbenzylphosphonium bromide; red, m. 172–4°.¹⁷
- Ph₃P:CHPh**. Not isolated, but detected by its reaction with water; from triphenylbenzylphosphonium bromide and sodium.¹²³
- Ph₃P:CC(C₆H₄-o)₂**. From triphenylphosphine and 9-bromofluorene in nitromethane, followed by treatment with alcoholic ammonia. Yellow plates, m. 253° (from EtOH).¹²⁹
- Et₃P·C(O):CPh₂**. From diphenylketene and triethylphosphine. Yellow mass, dec. 100°. Dissociates in solutions.¹⁴⁶

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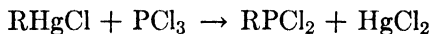
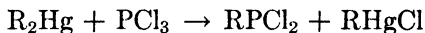
Halophosphines

The substances discussed in this chapter are the dihalophosphines, RPX_2 , and the monohalophosphines, R_2PX . The cyano and the thiocyno derivatives are also included, being regarded as simple derivatives of the halophosphines.

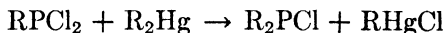
METHODS OF SYNTHESIS

I. Reaction of phosphorus trihalides (or dihalophosphines) with organic mercury compounds

After some unsuccessful earlier attempts,¹⁶ a number of aromatic and aliphatic dichlorophosphines have been prepared by heating phosphorus trichloride with the corresponding dialkylmercury or diarylmercury derivatives in sealed tubes for several hours to 180 to 230°. The reaction generally proceeds by a combination of the routes shown in the following equations.^{21, 53}



The reaction usually yields some monochlorophosphines as the by-products resulting from the continued action of the dichlorophosphines.²¹



This reaction, in turn, can be utilized for the synthesis of monochlorophosphines having the same or different radicals.⁶³

The use of phosphorus tribromide results in the formation of the corresponding bromophosphines.³²

A few instances of the deliberate use of alkyl(or aryl)-mercury halides, instead of compounds of R_2Hg type, have been reported.^{72, 79} Finally, a small yield of halophosphine has been reported from the use of triphenylantimony instead of diphenylmercury in this reaction.⁸

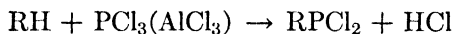
The high temperatures indicated above are not usually necessary for the reaction proper, but they serve the useful purpose of decomposition of residual RHgX compounds to mercuric chloride, which is filtered

off, usually after dilution by an inert solvent, prior to the distillation of the products. However, the removal of mercury is not complete, and all authentic reports of this reaction stress the great difficulty or impossibility of obtaining mercury-free preparations. Repeated fractionations and filtrations of the separated mercury are moderately effective, but these expedients invariably reduce the originally satisfactory yields (often 50 to 60%) to much lower figures. In spite of these difficulties, the method remains a very valuable one, especially for the determination of structures of compounds obtained by other methods (principally the Friedel-Crafts reaction).^{48, 53} The site of entry of the phosphorus atom is the location of the mercury in the starting material.

The side reactions in this method are somewhat repressed, and better yields are obtained if the phosphorus compound (PX_3 or RPX_2) is used in a substantial excess. (Michaelis.)

II. Reaction of aromatic compounds with phosphorus trihalides and aluminum chloride

This method, a variation of a conventional Friedel-Crafts reaction, may be represented in part by the following equation.



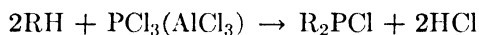
The reaction has been used for the preparation of a variety of aromatic phosphorus compounds as can be gleaned from the table of products at the end of this chapter. The notable failures of this reaction have been reported for stilbene, iodobenzene, benzonitrile, benzophenone, and ethyl benzoate.^{53, 54}

The reaction is conducted by refluxing (preferably with stirring) a mixture of the aromatic compound with phosphorus trichloride and anhydrous aluminum chloride. The old procedure devised by Michaelis⁵³ called for unduly long reaction time (up to 36 or more hours). This long time has been found to be unnecessary and even undesirable, for in fact most aromatic compounds, which react satisfactorily in the usual Friedel-Crafts reactions, give excellent conversions to dichlorophosphines (70 to 80%) in reflux periods of but 2 to 8 hours. Only the polyhalogenated, sluggishly reacting compounds require reaction periods of the order specified by Michaelis.^{17, 35}

Actually the original, arbitrarily specified, proportions of the reactants can be varied to a considerable extent. Large excess of either phosphorus trichloride or the aromatic component is beneficial in speeding the reaction and in keeping the mixture fluid. The amount of aluminum chloride, however, is quite important. It must be used in amounts

that exceed one-third of the molar proportion of the aromatic component (in instances in which phosphorus trichloride is used in excess, the other variant has not been explored in detail sufficiently). Reduction of the amount of aluminum chloride below this figure reduces the yield sharply. Larger amounts of aluminum chloride are of lesser import, in terms of the yields. The structure, or even the exact composition, of the resulting complexes of aluminum chloride with the halophosphines has not been definitely established, in contrast to the recent studies in analogous series of arsenic derivatives.⁴¹ It is probably correct to assume the formation of complexes of type $(R\text{PCl}_2)_3 \cdot \text{AlCl}_3$, which not only shows the reason for declining yields with low proportion of the catalyst but also correlates this reaction with the observed facts about the arsenic derivatives.

Although the early workers indicated the formation of diarylchlorophosphines in their long refluxing period procedures with a few aromatic compounds (notably toluene and xylenes), with the over-all reaction shown by the following equation:



the recent work showed not only that this reaction is a much more general one than previously supposed, and applicable to compounds capable of participating in the first step of the reaction, but that this reaction is more correctly represented as a continuation of the first step in which the dichlorophosphines are converted to the monochlorophosphines. The reaction gains in prominence with the longer periods of reflux, and conversions of 30 to 50% have been shown to be possible with reaction periods upward of 30 hours.³⁵ The amount of aluminum chloride used in the reaction has only a moderate effect on the yields of the second step; only very large amounts (2 moles) appear to exercise a repressive effect. With the information on hand it is impossible to state categorically whether this reaction involves the reaction of dihalophosphines with the residual aromatic compound or the disproportionation of dihalophosphines into phosphorus trichloride and diaryl monohalophosphines, catalyzed by aluminum chloride.

The main difficulty in this method for over seventy years has been the isolation procedure. The original and very ineffective technique of Michaelis involved the extraction of the cooled reaction mixture with a hydrocarbon solvent (usually petroleum ether) and distillation of the extract.⁵³ This procedure gave yields that in most optimistic reports ranged up to 25% of theory in some cases; in many instances the actual yields have been below 10% of theory after final purification.^{27, 50, 53, 72} Although an improvement of the yield has been reported

by resorting to vacuum distillation of the entire reaction mixture,²⁰ this improvement is only moderate and has the disadvantage of leaving behind an extremely unattractive residue in the apparatus. The loss of the major part of the yield in these procedures is caused by the halophosphine-aluminum chloride complex, and it was not until the recent work on satisfactory dissolution of this complex that the actual performance of the reaction was substantially improved.

One of these procedures, described in detail in Chapter 7, involves the direct conversion of the halophosphines into derivatives of phosphonic acids.³⁵

The other recent procedure has two variations.¹⁷ According to one of them, the cooled reaction mixture is treated, with adequate stirring, with an amount of water (either water as such or in the form of hydrochloric acid) equivalent to 3 moles per mole of aluminum chloride used in the reaction. After the addition the mixture is diluted with benzene or petroleum ether, and the readily filterable precipitate of hydrated aluminum chloride is removed. In the second variation 1 mole of phosphorus oxychloride is added to the reaction mixture for each mole of aluminum chloride in the mixture. After brief refluxing and dilution with petroleum ether, the aluminum is filtered off in the form of an equimolecular complex $\text{AlCl}_3 \cdot \text{POCl}_3$. This procedure offers the best possibility of actual isolation of monochlorophosphines from the Friedel-Crafts reaction; they have not been isolated as such by the original Michaelis isolation procedure. The two variants of removal of aluminum chloride complexes have been reported only in applications with benzene. There is little doubt, however, that the procedures are much more generally usable and depend solely on the lesser stability of the halophosphine complex in comparison with the water or the oxychloride complexes.

It should be noted that a high grade of anhydrous aluminum chloride should be used in this reaction, with the notable exception in the instance of alkyl ethers of phenol. They require the use of partly hydrated aluminum chloride, as the anhydrous substance causes substantial dealkylation, with the resulting phenol reacting with phosphorus trichloride to yield phenyl dichlorophosphite instead of the dichlorophosphine.^{36, 73}

The bulk of the published data on this reaction has been based on the low-efficiency extraction technique. For obvious reasons the current stock of information on the orientation of the entering atom of phosphorus with existing groups must be replenished by investigations of the new methods of isolation. The possible escape from detection in the older procedure is all too obvious for many isomeric products,

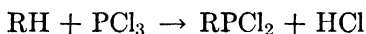
which might be formed in small amounts (or even moderately large ones). Thus chlorobenzene and phenol ethers are reported to yield only the para isomers. Bromobenzene appears to give the para isomer, but a second isomer of a phosphonic acid has been isolated from hydrolysis products of the untractable aluminum chloride complex (this isomer has never been identified as to structure). In experiments with toluene, the para isomer has been isolated by the method of freezing out the dichlorophosphine from a mixture with a lower melting material, presumed to be the ortho isomer. Xylenes (ortho and meta) give unresolved isomer mixtures of halophosphines. Resolutions have been accomplished in a few cases only after hydrolysis to the acids.^{53, 80}

Although phosphorus trichloride has usually been used, it is also possible to use phosphorus tribromide for the preparation of the bromophosphines; a few instances have been reported.³⁸

A successful use of this reaction with aliphatic compounds has been reported in patent literature. Petroleum fractions, containing hydrocarbons with six or more carbon atoms, are said to undergo the above reaction satisfactorily. Lower hydrocarbons give side reactions in which phosphorus is liberated. No individual substances have been reported.⁸¹ (Michaelis; Dye; Kosolapoff.)

III. Pyrolysis of aromatic compounds with phosphorus trichloride

This venerable reaction, which may be represented by the equation:



has been used with worth-while results only with benzene. Minute yields of apparently the meta-tolyl dichlorophosphine have been isolated from toluene,⁶² and a low yield of 2-thienyl derivative has been obtained from thiophene after a prolonged reaction.⁷⁵

The reaction consists of recycling a vapor mixture of phosphorus trichloride and benzene through a red-hot tube. Several forms of the apparatus have been devised, differing only in minor details of construction.^{1, 33, 37, 40, 46, 48, 62, 66, 72} Inert atmosphere (nitrogen or carbon dioxide is usually specified) is used for safety reasons. The tube proper is either a porcelain pipe or a combustion glass tube. A filling of broken porcelain is reported to give better yields than an empty tube.¹ Yields in a laboratory-size apparatus have been reported as high as 150 grams per day. This is much below the yields from the Friedel-Crafts reaction, but the conversions are fairly good. Volatile by-products, which include fragments of the hydrocarbons, free phosphorus, and some phosphines, are usually observed. A modification of the tube method is the use of a

glass jacket around a centrally located, electrically heated quartz tube that is kept at red heat.⁶ The product as obtained from the pyrolysis apparatus contains appreciable amounts of free phosphorus and phosphines, which can be removed by heating to 200° in sealed tubes for several hours,⁷ or by refluxing in inert atmosphere.^{1, 17, 72} (Michaelis.)

IV. Thermal decomposition of R_2PX_3 and R_3PX_2

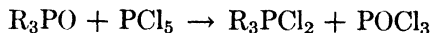
The decomposition of secondary and tertiary polyhalophosphines (phosphorus chlorides) by heat was observed many years ago,^{9, 68} but only recently has this reaction been utilized as a truly useful tool for synthetic purposes.⁷¹ The reaction may be shown by the following equations.



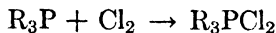
The second, and more valuable, variation can utilize compounds with like or unlike radicals and thus produce disubstituted monochlorophosphines of symmetric and unsymmetric types. The reaction is probably related to the much better studied thermal decomposition of true quaternary phosphonium halides. (Plets.)

The necessary R_2PCl_3 compounds for the first variant are made by addition of chlorine to dichlorophosphines. This variation does not appear to be an important one.

The necessary R_3PCl_2 compounds for the second variant are prepared in situ (they are usually poorly stable and cannot be stored conventionally). The preparation may proceed either by the reaction of tertiary phosphine oxides with phosphorus pentachloride:



or by addition of chlorine to tertiary phosphines:



The phosphine oxide procedure is used most satisfactorily with alkyl or aralkyl compounds, as the action of chlorine on these is usually attended by considerable decomposition and degradation. Although phosphorus pentachloride is the best reagent, other halides have been used with moderate success ($SOCl_2$, SO_2Cl_2 , $ClSO_3H$, $SiCl_4$).⁷¹ The chlorine procedure is carried out with cooling and in an inert solvent (CCl_4 , usually), and it may generally be used with aromatic compounds.

The resulting dichlorides are freed of the by-products that result from the synthesis by distillation, after which the residue is subjected

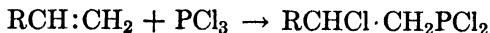
to heat sufficient to cause the desired decomposition. The resulting products are distilled directly from the reaction vessel in inert atmosphere (usually carbon dioxide) at bath temperatures of 150 to 220°, which suffice for all compounds studied so far. The higher members of the series are so treated under reduced pressure to effect the distillation. The heating must be gradual to prevent violence of decomposition. The distillate is fractionated to recover the products usually obtained in good yields (over 50% in most cases).

V. Heating phosphorus halides with alkyl halides

This reaction has but little application to this date. It has been found that phosphorus trihalides (PCl_3 and PBr_3) on being heated to the vicinity of 200° with alkyl halides (usually iodides) undergo a reaction that produces mono- and dihalophosphines, as well as a host of other products, including tertiary phosphines and the quaternary phosphonium halides. Usually phosphorus iodides give better results than the chloride or the bromide. The halophosphines have not been isolated as such, but have been oxidized to the corresponding phosphonic acids after hydrolysis. The dialkyl derivatives appear to be formed to the greatest extent when the molecular ratio of alkyl iodide to the phosphorus halide is three to one. The total yields are in the neighborhood of 20 to 40%, but they include all the by-products. The yields of individual substances are substantially lower.⁴ The reaction may be regarded as progressive replacement of halogens on the phosphorus atom by the alkyl radicals. (Auger.)

VI. Catalyzed addition of phosphorus trichloride to olefins

Only one specific instance is described in the literature. The mixture of an olefin (1-octene) with an excess of phosphorus trichloride in the presence of a substantial (over equimolar proportion) amount of acetyl peroxide, on being heated to 85° for several hours, gave a moderate yield of a dichlorophosphine, which had an atom of chlorine in the alkyl chain. Presumably the product formed by the addition of phosphorus trichloride in the form of Cl-PCl_2 across the double bond. The published requirements for this reaction are that the olefin must be an aliphatic compound and that the first carbon atom must have a hydrogen atom. The over-all reaction may be illustrated as follows:

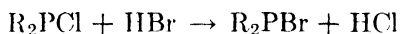
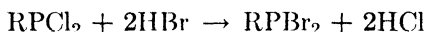


The mechanism of this reaction is presumed to go through the medium of free acetyl radical by chain mechanism. However, no confirmatory data have been published about this. It is also stated that the olefin-

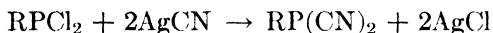
phosphorus trichloride mixtures undergo the addition reaction merely on illumination by ultraviolet light, presumably also by a chain mechanism.^{30, 31} The other mechanism alternative is the ion formation from phosphorus trichloride, under the conditions used, followed by addition of these to the olefin bond. (Kharasch *et al.*)

VII. Halogen exchange

The chlorophosphines obtainable by the other methods can be readily converted to the corresponding bromophosphines by passage of dry hydrogen bromide into the chlorophosphines, usually with heating. This has been the usual method of preparation of the bromophosphines listed at the end of this chapter. The reaction may be conveniently carried out by employing phosphorus tribromide as a solvent.^{32, 71}



The halophosphines can be converted to the corresponding cyano or thiocyno derivatives by heating, preferably in xylene solution, with the appropriate silver salts.^{53, 71} (Michaelis; Plets.)



VIII. Reaction of dialkylanilines with phosphorus trichloride

Although the original studies of Michaelis and his students used aluminum chloride catalyst in this reaction, subsequent work showed that the anilines can react with phosphorus trichloride without the added catalyst, provided that an excess of the amine is used sufficient to bind the resulting hydrogen chloride. By using the appropriate amounts of the dialkylanilines, at least 2 moles per mole of the trichloride, substitution of one, two, or all three chlorine atoms is effected so that in practice the reaction mixture of this type, after the usual period of reflux, represents a mixture of the monohalophosphines, dihalophosphines, and the tertiary phosphines. No halophosphines have been specifically isolated by this procedure, but the reaction mixtures have been hydrolyzed to yield the corresponding phosphorus acids.⁵

The first step may be represented by:

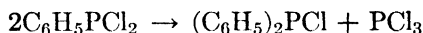


A reaction that has considerable similarity occurs on heating diphenylamine with phosphorus trichloride to approximately 200°. No halo-

phosphines have been isolated directly from this reaction, but the hydrolysis products include a cyclic acid that could have resulted from a corresponding cyclic chlorophosphine formed by a two-step ring closure in ortho position to the nitrogen atom. The chlorophosphine proper has been prepared by procedure XIII from this product of hydrolysis.^{67, 76} (Michaelis; Bourneuf; Sergeev.)

IX. Pyrolysis of dichlorophosphines

Phenyldichlorophosphine, on being heated in sealed tubes for many hours at 300°^{7, 14, 58} or in bomb tubes at similar temperature,¹ disproportionates into diphenylchlorophosphine and phosphorus trichloride.



The reaction is not suitable for substituted derivatives as isomerization occurs.⁵⁴ It must be noted that triphenylphosphine does not show disproportionation on similar heating with phosphorus trichloride.⁶⁸ (Broglie; Michaelis.)

X. Halogenation of primary and secondary phosphines

Although the usual scientific literature states emphatically that the action of halogens, like chlorine, upon primary and secondary phosphines results in decomposition of these substances, a recent patent discloses the successful application of direct halogenation of aliphatic phosphines by resorting to inert solvents and low temperatures (usually below 20°). Presumably controlled amounts of the halogen are used to prevent further action (addition), and all the principal halogens are stated to be effective (chlorine, bromine, and iodine).^{77, 78} (Walling.)



XI. Conversion of phosphonous acids to dihalophosphines

Although dihalophosphines yield phosphonous acids on hydrolysis, the reverse transformation has been reported in only one instance.²² The triphenylmethyl derivative used in this case was converted in good yield into the corresponding dichlorophosphine by prolonged boiling, in nitrogen atmosphere, with phosphorus trichloride. It is of great interest to investigate the possibilities of this transformation with other compounds, for both practical and theoretical reasons. The triphenylmethyl compound cited above is a rather unusual one that shows considerable dissociation into radicals, and therefore cannot be cited as an example of typical behavior.

XII. Reaction of phosphines with phosgene

Phenyldichlorophosphine has been prepared by passage of phosgene into warm phenylphosphine.⁵⁷ It is possible that the reaction is a general one for compounds having a phosphorus-hydrogen bond.



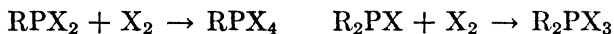
XIII. Reaction of phosphinous acids with thionyl chloride

A reverse transformation of a hydrolysis product of a halophosphine into the halophosphine has been reported for a complex product; the phosphinous acid based on dihydrophenophosphazine ring has been converted to the chlorophosphine by warming with thionyl chloride.⁷⁶

REACTIONS AND GENERAL CHARACTERISTICS

The halophosphines are usually liquids having sharply unpleasant phosphine-like odor (probably caused by partial hydrolysis in the atmosphere with attendant phosphine formation). They are capable of many of the usual addition reactions characteristic of trivalent phosphorus compounds, and, in addition, being essentially acid halides, they are capable of many replacement reactions that involve the highly reactive halogen atoms. The reactions proper are discussed in more detail in sections pertaining to the appropriate reaction products. The general summary of the reactions shown below has been gathered largely from the information of some considerable age obtained with phenyl dichlorophosphine and diphenyl chlorophosphine, which have been the most popular subjects for investigations.

Addition of halogens results in the corresponding mono- or disubstituted phosphorus tetrahalides or trihalides.^{21, 43, 46, 48, 53, 56}

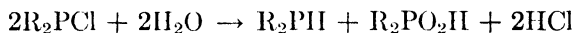


In this, as in other reactions, the disubstituted monohalophosphines show a greater tendency for addition reactions than the monosubstituted dihalophosphines, in common with the general principle of closer similarity to true tertiary phosphines.⁵⁴

Oxidation of the halophosphines results in the formation of the corresponding phosphonyl halides, RPOX_2 and R_2POX , respectively. In practice, however, this reaction is rather difficult to carry out with satisfactory yields, and direct oxygenation is not a good method in its present state for the preparation of these useful substances.⁴⁸ The addition of sulfur results in the formation of the corresponding thionophosphonyl halides,^{21, 32, 60} RPSX_2 and R_2PSX ,⁴² respectively; these

are also obtainable by heating the halophosphines with sulfur monochloride^{33,60} or thiophosphoryl chloride.¹⁹

Hydrolysis of dihalophosphines yields the corresponding phosphonous acids, RPO_2H_2 .^{21,53,59} However, the hydrolysis is usually accompanied by a certain amount of the typical disproportionation of the phosphonous acids into the phosphonic acids and phosphines. This is particularly apparent in hydrolysis of secondary monohalophosphines, which, especially in alkaline solutions, form only the corresponding phosphonic acids, with attendant variable amounts of the corresponding phosphines. Only the highly substituted monohalophosphines, which have been reported from only one source,⁷¹ appear to give essentially the hydrolytic reaction without attendant oxidation or disproportionation. These notable exceptions are the *p*-nitro and the *p*-dimethylamino derivatives of diphenylchlorophosphine, provided that water is used for hydrolysis. In alkaline solutions the secondary reaction is always apparent. The reactions of such disproportionation may be shown by the following over-all equation.^{14,58,71}



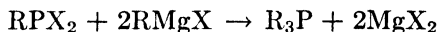
The reaction of halophosphines with alcohols generally leads to the same result as obtained with water (see above), as the resulting esters are largely hydrolytically decomposed by the hydrogen halide.³⁴ Phenols appear to yield esters, especially with the monohalophosphines.⁵⁴

The use of alkali alkoxides in the above reaction or the use of the alcohols in the presence of a tertiary base, such as pyridine or dimethylaniline, yields the esters in good yields. The reaction is best conducted with the tertiary bases. Similar results are obtained with the mercaptans.^{1,2,34,71} These reactions, especially when conducted with alkali derivatives, also result in variable yields of the isomerization products of the esters or the thioesters. These compounds are discussed in the chapters dealing with phosphonic acids and phosphine oxides and sulfides.

In common with other acid halides, the halophosphines react with ammonia and amines to produce amides. The products obtained in such reactions are discussed in Chapter 10.^{21,53,55,64}

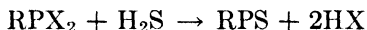
Replacement reactions in which the chlorine atoms of mono- and dichlorophosphines are replaced by cyano, thiocyno, or bromo groups have been already discussed in the section on syntheses.^{44,53,60,71} Similarly the reaction with organomercury compounds is referred to that section.

Reactions of halophosphines with Grignard reagents and dialkylzinc compounds result in the formation of tertiary phosphines.^{27,44,48}



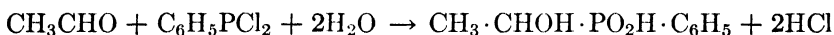
The reaction of dihalophosphines with phosphine yields a complex that has been assigned the structure $(\text{RPhCl})_2\text{P}$.⁴⁷ Very little is known about the mode of this reaction, however, and the intermediate shown above may have a more complex formulation.

The reaction of dihalophosphines with hydrogen sulfide results in the formation of products that are best regarded as derivatives of thio- and dithiophosphonic acids.³² Thus the reaction products of boiling phenyl-dichlorophosphine and hydrogen sulfide are substances that on oxidation and hydrolysis give diphenylphosphonic acid and are assigned the structures $\text{R}_2\text{PSP:S}$ and $\text{R}_2\text{PS}\cdot\text{S}\cdot\text{SPR}_2$. It appears that the primary products that might be expected, that is, products resulting from a reaction



undergo either an isomerization or further condensation to yield the final products depicted above.

The halophosphines react with aldehydes, forming adducts that on hydrolysis yield hydroxyphosphonic acids.⁵³ The reaction with unsaturated ketones has been also explored in more recent times. The results of these reactions are embodied in Chapter 7, dealing with phosphonic acids. The over-all course of such a reaction may be shown by the following equation:



It must be realized that the reactions cited above are merely the over-all results. The actual mechanisms and the possible intermediate substances remain a matter of speculation. It is highly possible that the trivalent phosphorus atom plays a significant role in the primary steps of these conversions. For example, the apparent rearrangements or isomerizations involved in the action of hydrogen sulfide are totally unexplored in the detailed manner.

HALOPHOSPHINES

DIHALOPHOSPHINES

EtPCl₂. I. b. 114–7°, d^{19} 1.2952.^{21, 51}

PrPCl₂. I. b. 140–2°, d^{19} 1.1771.²¹

iso-PrPCl₂. I. b. 135–8°, d^{23} 1.2181.²¹

BuPCl₂. I. b₇₆₀ 157–60°. ¹⁵

BuPBr₂. X. b₁₀ 80–95°. ⁷⁷

iso-BuPCl₂. I. b. 155–7°, d^{23} 1.1236.²¹

iso-AmPCl₂. I. b. 180–3°, d^{23} 1.1024.^{21, 51}

- Me(CH₂)₅CHCl·CH₂PCl₂.** VI. b_{0.5} 85–8°. ³⁰
- PhPCl₂.** I. ^{46, 48} III. ^{1, 6, 17, 33, 37, 40, 46, 48, 72} II. ^{17, 27, 50} IV. ⁵⁷ b. 225°, ¹ b. 222°, ⁵⁰ b₆₇ 140–2°, ⁶¹
b. 221–2°, ²⁶ d₄⁰ 1.341, ¹ d₄⁰ 1.3428, d₄²⁰ 1.319, n_D⁷ 1.60533. ⁸²
- PhPBr₂.** I. ^{32, 48, 60} VII. ^{32, 48, 60} b. 255–7°. ^{32, 48, 60}
- PhPI₂.** Obtained only as HI salt, a crude solid; VII. ^{37, 48}
- PhP(CN)₂.** VII. ⁵³ b₂₀ 144–5°. ⁵³
- PhP(SCN)₂.** VII. ⁵³ b₂₀ 205–7°. ⁵³
- 4-ClC₆H₄PCl₂.** II. ^{53, 70} b. 253–5°, ⁵³ b₂₀ 133°, ⁷⁰ d¹⁷ 1.425. ⁵³
- 4-BrC₆H₄PCl₂.** II. ^{11, 26, 53} b. 271–2°, ⁵³ b₁₃ 139°, ¹¹ b₁₄ 135–6°, ²⁸ b₂₁ 147–8°, d¹⁵ 1.6895. ⁵³
- 4-Me₂NC₆H₄PCl₂.** II. ⁶⁷ VIII. ⁵ m. 66°, b₁₂₀ 250°. ⁶⁷
- 4-Et₂NC₆H₄PCl₂.** II. Undistillable oil. ⁶⁷
- 4-(PhCH₂)MeNC₆H₄PCl₂.** II. Undistillable oil. ⁶⁷
- 4-(PhCH₂)EtNC₆H₄PCl₂.** II. Undistillable oil. ⁶⁷
- 4-MePhNC₆H₄PCl₂.** II. Oil that decomposes at 200°. ⁶⁷
- 4-MeOC₆H₄PCl₂.** I. ⁷³ II. ^{11, 23, 26, 28, 36, 53} b. 245–53°, ²³ b₂₁ 153°, ²⁸ b₁₈ 150°, ²³ b₁₃ 150°, ¹¹
b₁₁ 140–1°, ²⁸ d₀⁰ 1.3604, d₀¹⁵ 1.3468, ²⁸ d₀²⁶ 1.331. ²³ The original constants ⁵³ were obtained with grossly impure product: b₁₂ 130°, d¹⁵ 1.0764.
- 4-ETOC₆H₄PCl₂.** I. ⁵³ II. ⁵³ b. 266°. ⁵³
- 4-PhOC₆H₄PCl₂.** II. b₁₂ 200°, d₄²⁰ 1.3122. ^{12, 26}
- PhCH₂PCl₂.** I. b₁₂ 110–1°. ²⁵
- 2-MeC₆H₄PCl₂.** Apparently a by-product in II. I. ^{53, 66} b. 244°, d¹⁸ 1.3067.
- 3-MeC₆H₄PCl₂.** I. ⁵³ Apparently forms in III. ⁶² b. 235°, d²² 1.282. ⁵³
- 4-MeC₆H₄PCl₂.** I. ⁶⁶ II. ^{26, 38, 50, 53, 62, 65, 66, 74, 79} m. 25°, b. 245°, ⁶⁸ b₁₂ 100°. ²⁶
- 2-Cl-4-MeC₆H₃PCl₂.** II. b. 265–6°, d²² 1.373. ⁴⁵
- 4-MeC₆H₄PBr₂.** II. ³⁸ m. 160–1°. ³⁸
- 4-MeC₆H₄P(CN)₂.** VII. b₅₀ 145°. ⁵³
- 4-MeC₆H₄P(SCN)₂.** VII. b₄₀ 237–40°. ⁵³
- 1,2-Me₂C₆H₃-X-PCl₂.** Isomer mixture. II. ^{53, 66, 80} b. 278°. ^{53, 66, 80}
- 2,4-Me₂C₆H₃PCl₂.** I. ⁸⁰ b. 256–8°. ⁸⁰ II gives a mixture, b. 265°, with the 3,5-isomer. ⁶⁶
- 2,5-Me₂C₆H₃PCl₂.** II. ^{24, 26, 66, 80} b. 253–4°, ^{66, 80} b₁₆ 133°, ²⁶ b₁₂ 129°, ²⁴ b₂₃ 140°, ²⁴
d₁₈¹⁵ 1.25. ^{66, 80}
- 4-EtC₆H₄PCl₂.** II. ^{23, 26, 53} b. 250–2°, ⁵³ b₁₈ 133°, ²⁶ b₁₂ 127°, ²³ d¹⁷ 1.227, ⁵³ d₄²⁵ 1.225. ²³
- 2,4,5-Me₃C₆H₂PCl₂.** I. ⁵³ II. ⁵³ b. 280°, d²⁰ 1.2356. ⁵³
- 2,4,6-Me₃C₆H₂PCl₂.** II. ^{10, 53} m. 35–7°, ⁵³ b. 273–5°, ⁵⁸ b₁₆ 156–7°, ¹⁰ d¹⁵ 1.205.
- 4-iso-PrC₆H₄PCl₂.** II. ^{26, 53, 69} b. 268–70°, ⁵³ b₁₄ 132–4°, ²⁶ b₁₀ 125–7°, ⁶⁹ d¹² 1.190. ⁵³
- 1-Me-4-iso-PrC₆H₃-2-(or 3)PCl₂.** II. b. 275–8°, obtained crude. ⁵³
- PhC₆H₄PCl₂.** II. Mixture of isomers; m. 5°, b₁₀ 200–20°, d¹⁴ 1.3098. ^{40, 54}
- 4(?)-(PhCH₂)C₆H₄PCl₂.** II. b₂₀ 221°, d¹⁷ 1.182. ⁵⁴
- 4(?)-(PhCH₂CH₂)C₆H₄PCl₂.** II. b₆₀ 250°, m. 2°. ⁵⁴
- Ph₃CPCl₂.** XI. m. 138–40°, decomp. 240°. ²²
- 1-C₁₀H₇PCl₂.** I. ³⁹ II. ³⁹ b. over 360°, ²⁹ b₁₀ 180°, m. 58–9°. ³⁹
- 1-C₁₀H₇PBr₂.** II. ³⁹ m. 65–8°. ³⁹
- 2-C₁₀H₇PCl₂.** I. m. 50–60°, b_{9–10} 180°. ³⁹
- Dibenzofuran-3-dichlorophosphine.** II. b₂₅ 245–50°. ¹³
- 2-Thienyldichlorophosphine.** III. b. 218°. ⁷⁵

MONOHALOPHOSPHINES

- MeEtPCl.** IV (from MeEt₂PCl₂). b₁₅ 49–51°, b. 157–60°. ⁷¹
- MeEtPBr.** VII. b₁₅ 81–8°. ⁷¹
- MeEtPCN.** VII. Needles, m. 37–41°. ⁷¹

MeEtPSCN. VII. Needles, m. 59–62°. ⁷¹

Et₂PCl. IV. ^{9,71} b₁₅ 60–70°. ⁷¹

Et₂PBr. VII. b₁₅ 130–5°. ⁷¹

Et₂PCN. VII. Needles, m. 42–3°. ⁷¹

Et₂PSCN. VII. Needles, dec. 67–9°. ⁷¹

Pr₂PCl. IV. b₁₅ 99–101°. ⁷¹

Pr₂PBr. VII. b₁₅ 143–7°. ⁷¹

Pr₂PCN. VII. Needles, dec. 81–3°. ⁷¹

Pr₂PSCN. VII. Needles, m. 71–5°. ⁷¹

Bu₂PCl. IV. b₁₅ 120–5°. ⁷¹

Bu₂PBr. VII. ⁷¹ X. ⁷⁸ b₁₅ 156–8°, b₁₀ 126–8°. ⁷⁸

Bu₂PCN. VII. Needles, m. 89–92°. ⁷¹

Bu₂PSCN. VII. Plates, m. 78–82°. ⁷¹

(Note. Michaelis' diacetyl chlorophosphine ⁵² is not a chlorophosphine but a phosphonyl chloride. See Chapter 4 on phosphonyl halides.)

MePhPCl. IV (from Me₂PhPCl₂). b₁₅ 150–65°. ⁷¹ Earlier preparation was erroneous. ⁴⁴

MePhPBr. VII. b₁₅ 200–5°. ⁷¹

MePhPCN. VII. m. 61°. ⁷¹

MePhPSCN. VII. b₁₅ 98–100°. ⁷¹

EtPhPCl. IV (from Et₂PhPCl₂). b₁₅ 180–90°. ⁷¹

EtPhPBr. VII. b₁₅ 220–5°. ⁷¹

EtPhPCN. VII. Needles, m. 72–3°. ⁷¹

EtPhPSCN. VII. b_{2,5} 69–70°. ⁷¹

Ph₂PCl. I. ^{44, 49, 61, 63} IV. ^{68, 71} IX. ^{1, 7, 14, 18} b. 320°, ¹⁴ b. 316–20°, ¹⁸ b₅₇ 210–5°, ⁶¹ b₁₆ 179–80°, ⁴⁴ b₁₄ 178°, ¹ b₁₃ 175–6°, ³ d₀¹⁵ 1.2295. ¹

Ph₂PBr. VII. b₁₈ 183–4°. ^{44, 71}

Ph₂PCN. VII. Needles, m. 39–40°, b₁₅ 170–5°. ⁷¹

Ph₂PSCN. VII. b₁₅ 270–80°. ⁷¹

(4-BrC₆H₄)PhPCl. I. b₁₁ 203–4°. ¹¹

(4-MeOC₆H₄)PhPCl. I. b_{0,15} 149–52°, b_{0,03} 137°. ¹¹

(2-ClC₆H₄)₂PCl. IV. m. 37°, b₁₅ 253–7°. ⁷¹

(2-ClC₆H₄)₂PBr. VII. b₁₅ 280–90°. ⁷¹

(2-ClC₆H₄)₂PCN. VII. Plates, m. 52°. ⁷¹

(2-ClC₆H₄)₂PSCN. VII. b₂ 110–5°. ⁷¹

(4-ClC₆H₄)₂PCl. IV. m. 6–8°, b₁₅ 260–5°. ⁷¹

(4-ClC₆H₄)₂PBr. VII. Plates, m. 47–8°, b₁₅ 300–10°. ⁷¹

(4-ClC₆H₄)₂PCN. VII. Plates, m. 101–2°. ⁷¹

(4-ClC₆H₄)₂PSCN. VII. Crystals, dec. 120°. ⁷¹

(4-O₂NC₆H₄)₂PCl. IV. Plates, m. 91–3°, b. over 370°. ⁷¹

(4-O₂NC₆H₄)₂PBr. VII. Red, m. 117–20°. ⁷¹

(4-O₂NC₆H₄)₂PCN and the SCN analog could not be prepared. ⁷¹

(4-Me₂NC₆H₄)₂PCl. IV. m. 16–18°, b₁₅ 210–5°. ⁷¹

(4-Me₂NC₆H₄)₂PBr. VII. Orange crystals, m. 102°. ⁷¹

(4-MeC₆H₄)PhPCl. I. ^{54, 72, 74, 79} IV. ⁷¹ b. 340°, ⁵⁴ b₁₀₀ 230–40°. ⁷¹

(4-MeC₆H₄)PhPBr. VII. b₁₅ 270–80°. ⁷¹

(4-MeC₆H₄)PhPCN. VII. m. 37–8°. ⁷¹

(4-MeC₆H₄)PhPSCN. VII. Obtained as crude crystals; red. ⁷¹

(2-MeC₆H₄)₂PCl. IV. m. 4°, oil. ⁷¹

- (2-MeC₆H₄)₂PBr.** VII. b₁₅ 210–2°. ⁷¹
(2-MeC₆H₄)₂PCN. VII. m. 57–60°. ⁷¹
(2-MeC₆H₄)₂PSCN. VII. Undistillable oil. ⁷¹
(4-MeC₆H₄)₂PCl. I. ⁵⁴ IV. ⁷¹ b. 345–50°. ^{54, 71}
(4-MeC₆H₄)₂PBr. VII. b₁₅ 260–70°. ⁷¹
(4-MeC₆H₄)₂PCN. VII. b₁₅ 150–3°, m. 10–2°. ⁷¹
(4-MeC₆H₄)₂PSCN. VII. b₁₅ 230–2°. ⁷¹
(2,4,5-Me₃C₆H₂)PhPCl. I. b. 356°, ^{49, 63} b₁₀ 208°. ⁵⁴
(2,4,5-Me₃C₆H₂)PCl. II. Crude; b. 305°. ^{53, 54}
(1-C₁₀H₇)₂PCl. IV. b₁₅ 270–80°. ⁷¹
(1-C₁₀H₇)₂PBr. VII. m. 29–30°, b₁₅ 280–300°. ⁷¹
(1-C₁₀H₇)₂PCN. VII. Needles, dec. 129°. ⁷¹
(1-C₁₀H₇)₂PSCN. VII. m. 68–70°. ⁷¹
5,10-Dihydro-10-chlorophenophosphazine. XIII. Yellow oil. ⁷⁶

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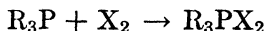
Halophosphine Halides and Phosphonyl Halides

The compounds discussed in this chapter may be represented by the general formulas RPX_4 , R_2PX_3 , R_3PX_2 , RPOX_2 , R_2POX , and by the thiono and seleno analogs of the last two types. They represent halogen derivatives of phosphorus in its higher oxidation state that contain one or more radicals bound to the central atom by carbon to phosphorus bonds. Although the quaternary phosphonium salts are, strictly speaking, in the same general category on the basis of such formulas, their chemical reactions set them apart from the above compounds. They are given a separate treatment in the following chapter. The ester halides of phosphonic acids are included in this chapter because of their essentially acid halide reactivity.

METHODS OF PREPARATION

I. Addition of halogen to the corresponding trivalent compounds

The affinity of trivalent phosphorus derivatives for halogens permits a convenient preparation of compounds of the general types RPX_4 , R_2PX_3 , and R_3PX_2 from the corresponding primary and secondary halophosphines and tertiary phosphines.^{26, 51-54, 57, 62, 63, 65, 68, 69}

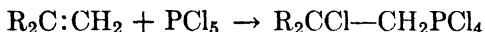


The halophosphines are best treated with the halogen (chlorine or bromine) in a suitable solvent with cooling and agitation. Solvents such as carbon tetrachloride or tetrachloroethane are usually best. Cooling is necessary, as a rule, to control the rather exothermic action. Agitation is of advantage because the products frequently separate from the solvent in the solid state. The reaction with tertiary phosphines must be conducted with good cooling, and, generally, only the triaryl members may be used. Phosphines with aliphatic groups are attacked by the halogens (chlorine has been generally used), and, unless they are diluted by a solvent and the halogen is similarly diluted, this

reaction is not suitable for such compounds. The products are isolated by careful evaporation of the solvent under anhydrous conditions. (Michaelis; Plets.)

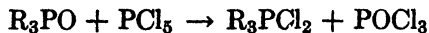
II. Addition of phosphorus pentachloride to olefins

Phosphorus pentachloride adds readily to selected olefins, in the sense Cl-PCl_4 , to form chloro-substituted aliphatic derivatives of the type R-PCl_4 . This reaction has been used primarily for the synthesis of the phosphonic acids that result from hydrolysis of such products. For this reason very few tetrachlorides have been specifically isolated in the pure state and characterized. The reaction consists, in essence, of the addition of the olefin (acetylene derivatives react similarly) to a finely divided suspension of the pentachloride in an inert solvent; benzene has been used as a rule. After being stirred for several hours, the resulting suspension of the adduct can be filtered. Usually no further purification is made because the solubility characteristic of the products is very similar to that of phosphorus pentachloride. An excess of the olefin serves to reduce a residuum of the latter to small amounts. The reaction is discussed in more detail in Chapter 7. It will suffice to state at this time that the structural requirements of the olefin are important; as a rule, only 1,2-olefins react. Steric hindrance of the ortho groups on aromatic nuclei attached to the 2-carbon is also of importance. It is interesting to note that indene, which is not a 1-2 olefin, reacts readily, probably because of the "exposed" position of its double bond. In the case of indene, the chlorine of the primary adduct may be removed as hydrogen chloride on refluxing in benzene, to give the over-all result of the substitution of hydrogen by PCl_4 group.² The general scheme of the reaction is shown below.^{8, 9, 38, 47, 76} (Bergmann.)



III. Reaction of tertiary phosphine oxides with phosphorus pentachloride

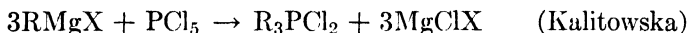
Although the formation of compounds of the general type R_3PX_2 in reactions of tertiary phosphine oxides with phosphorus pentachloride was indicated many years ago,^{15, 25} the practical aspects of this method were not developed until comparatively recently.⁶⁹ The over-all result may be shown as¹⁶



The reaction is most suitable for phosphine oxides that contain an aliphatic R group. It is conducted by gradual mixing of the reagents, followed by brief and gentle warming and distillation of phosphorus oxychloride under reduced pressure. The product usually crystallizes on cooling. Since compounds of this type are attacked by moisture and are unstable in storage or in prolonged heating, they are usually immediately utilized for further reactions. Thionyl chloride may be used in place of phosphorus pentachloride, and then the by-product is sulfur dioxide. The yields, however, are somewhat lower. Sulfur monochloride also acts in a similar manner, but the products are badly contaminated.⁶⁹ The use of chlorine has been reported in a similar reaction,¹⁰ but chlorine cannot be used with aliphatic derivatives.⁶⁹ (Plets.)

IV. Reaction of Grignard reagents with phosphorus pentachloride

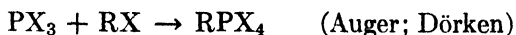
The reaction of phenylmagnesium bromide and analogous RMgX compounds leads, as has been mentioned earlier, to a spectrum of substitution derivatives, among which some triphenylphosphorus dichloride has been found. The reaction may be written as follows.³⁵



The reaction does not appear to have advantages over the more conventional procedures that give more clearly defined products.

V. Addition of organic halides to halophosphines

The halides of phosphorus represent the lowest rung in the reactivity scale of trivalent phosphorus compounds in respect to addition reactions, specifically, in this case, with alkyl types of halides. When phosphorus trichloride or tribromide is heated to 200° with alkyl halides (iodides are most reactive), a low yield, generally below 10% in several hours, of halophosphine derivatives is secured. These were not isolated as such, but were immediately converted to the acids. The use of phosphorus iodide, which is more reactive, gave poor yields (although somewhat higher than above) of similar derivatives. Since the high temperatures necessary for the reaction are conducive to cleavage and disproportionation, it is difficult to assign the true reaction course, which may involve a simple exchange of halogen for alkyl or may proceed by addition.⁷

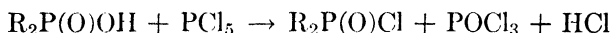


However, when diphenylchlorophosphine is used in a similar reaction with selected active halides, the addition course of the reaction becomes

quite clear. Clear-cut dihalides of type Ph_2RPX_2 were obtained in sealed tube reactions with benzyl halides at the temperatures near 180° .^{19,64} The increased tendency for addition reactions upon approach to the phosphine structure is evident.²¹

VI. Conversion of phosphonic acids to phosphoryl halides

Many of the most convenient methods of preparation of the compounds of the general class of phosphonic acid derivatives do not go through the formation of phosphoryl halides, but rather give the acids directly. In such cases the halides can be readily formed from the free acids by warming the acids with phosphorus pentachloride, using one mole of the phosphorus pentachloride for each hydroxyl available in the acid. (Michaelis.)



The products are isolated by distillation, usually in vacuo, after similar removal of phosphorus oxychloride. Usually the pentachloride is added gradually to the acid, and the mixture is warmed gently until the evolution of hydrogen chloride ceases.^{30,52} Acids with hydroxy-substitution on one-carbon are usually converted to the corresponding chloro derivatives,²² although dehydrohalogenation to the unsaturated derivatives may take place, especially if the phosphorus atom is on a secondary carbon atom.²⁷ Thionyl chloride may be effectively used in the place of phosphorus pentachloride, especially for the secondary phosphonic acids. In this case the by-products are sulfur dioxide and hydrogen chloride.^{23,27} Any carboxylic groups in the original acids are converted to the acyl chloride groups in a simultaneous action.

VII. Partial hydrolysis of compounds of types R_2PX_3 and RPX_4

Careful hydrolysis by limited amount of water converts the tetra- and the trihalides into the corresponding phosphoryl halides. Reactions of this type take place upon exposure of the halides to moist air. Since the phosphoryl halides are much less subject to hydrolytic attack than the polyhalides, a more or less effective preparation of the former may be achieved. The reaction has not been applied to any great extent because of the obvious difficulties of technique.^{51, 52, 54, 60, 69}

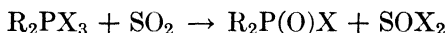
A much more effective preparation is achieved when organic acids, such as acetic or oxalic, are used. Then the polyhalides convert the organic acids into the corresponding halides in a smooth reaction, which needs but slight warming for completion, and the acyl halides and the

phosphonyl halides are recovered very satisfactorily by distillation, usually in vacuo.⁵¹ (Michaelis.)



VIII. Reaction of compounds of types RPX_4 and R_2PX_3 with sulfur dioxide

This reaction is probably the most convenient laboratory method for the conversion of the polyhalides into the corresponding phosphonyl halides. The general course of the reaction may be shown as follows:



The technique of the reaction is very simple. The polyhalide is dissolved, or suspended, in an inert solvent, and sulfur dioxide is bubbled into the stirred mixture until the reaction is complete. The reaction is rapid, and the product may be easily recovered by distillation.^{26, 51, 52, 54, 57, 62} (Michaelis.)

IX. Reaction of esters of phosphonic acids with phosphorus pentachloride

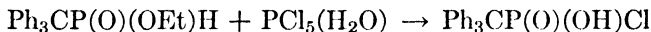
Esters of phosphonic acids, which are frequently more readily obtained in direct reactions than the free acids, may be converted to the corresponding phosphonyl chlorides by reaction with phosphorus pentachloride at elevated temperatures.⁷⁰ (Kabachnik; Hatt.)

Although an over-all equation may be written as follows:



it is most probable that the reaction is much more complex and, in the final analysis, may involve the formation of various intermediates in which polyphosphonate structures predominate. Usually the temperatures required for the completion of the reaction are in excess of 100° , and more probably lie in the neighborhood of 150° .^{33, 34} The use of lower temperatures is likely to cause the conversion of but one ester group into the halide.^{33, 34} Procedures of this type have been used on the crude polymeric esters of 2-chloroethanephosphonic acid, obtained by self-isomerization of the corresponding phosphites, with good results. Either sealed tubes or the usual apparatus may be used. A rather unusual case of this reaction arises with the monoethyl ester of triphenylmethanephosphonous acid; it yields triphenylmethanephos-

phenyl monochloride after the reaction with the pentachloride, followed by aqueous treatment.²⁹ It appears that the ordinarily unreactive hydrogen in compounds of this type is converted in this case to the active form, probably by substitution for chlorine.²⁹

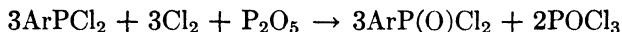


X. Oxidation of halophosphines

A few aryldichlorophosphines, notably the phenyl derivative, have been oxidized to the corresponding phosphonyl dichlorides, by the action of air or oxygen.^{29, 51, 69} The reaction is rather hazardous unless all traces of free phosphorus are absent, and it requires rather drastic conditions of time and temperature.⁵² No quantitative information is on hand for the procedures necessary for high-yield operation, as the ordinary bubbling of the gas into the starting material does not give good conversions. The secondary monochlorophosphines, R_2PCl , are oxidized fairly readily by air or oxygen on ordinary exposures, and the corresponding phosphonyl chlorides may usually be found to accompany the phosphines in the common methods of preparation of the phosphines. Air blowing, under anhydrous conditions, with moderate warming has been successfully used for the preparation of several secondary phosphonyl chlorides in this manner.⁶⁹ It may be noted that the *p*-dimethyl-amino derivative did not yield a pure product.⁶⁹ (Michaelis.)

XI. Reaction of dihalophosphines with chlorine and phosphorus pentoxide

Chlorination of a slurry of phosphorus pentoxide in a dihalophosphine has been reported to give good yields of the phosphonyl dihalide in accord with the following over-all equation: ^{75, 77}



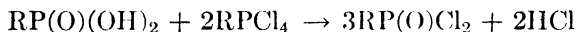
The reaction is best conducted with a slight excess of the pentoxide over the requirements of the above equation. It is run at the temperature spontaneously achieved by the mixture, usually 130 to 150° in the reaction vessel, for unsubstituted aryl derivatives, and at 30 to 40° for substances with aliphatic groups to avoid the chlorination which can occur at higher temperatures.⁷⁷

A similar reaction converts the tetrachloro derivatives, which are obtained by the reaction discussed in Section II, directly into the phosphonyl dihalides of the unsaturated type.⁷⁶ (Toy.)



XII. Reaction of phosphonic acids with compounds of type RPX_4

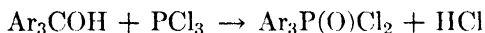
Primary phosphonic acids, generally the aryl members, may be converted to the corresponding phosphonyl dichlorides by reaction with the corresponding arylphosphorus tetrahalides (usually chlorides).⁴¹ The reaction requires the use of two moles of the tetrahalide for each mole of the primary phosphonic acid, as shown below.⁶⁶



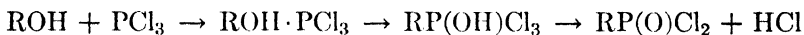
If the amount of the tetrahalide is reduced, the predominant action results in the formation of the metaphosphonic derivatives RPO_2 . The reaction is conducted similarly to the reaction with phosphorus pentachloride (see Section VI), to which it is obviously related. (Michaelis.)

XIII. Reaction of triarylmethyl carbinols with phosphorus trichloride

This curious reaction may be shown roughly by the following equation:



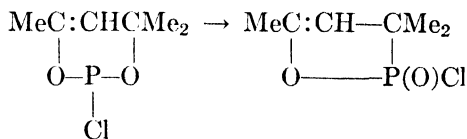
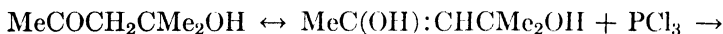
Instead of the expected dichlorophosphite, $ROPCl_2$, the product is a phosphonyl dichloride, which forms immediately in the course of the reaction. The same product results from potassium derivatives of the carbinols.²⁹ It is evident that the reaction either proceeds in these carbinols by the way of formation of the dichlorophosphite, which instantaneously rearranges to the final product (a possibility that is supported by the ready dissociation of such compounds), or goes by the way of coordination to the trivalent phosphorus, followed by formation of an abnormal adduct, owing to ionization of the carbinol in the sense $R-OH$.¹² (Boyd; Hatt; Arbuzov.)



The ionic hypothesis appears to have some direct support, in that a series of triarylmethyl carbinols arranged in the ascending order of "basicity" yield, on immediate hydrolysis with water, progressively increasing amounts of the corresponding phosphonic acids.¹³

The reaction is conducted by addition of the carbinol to the phosphorus trichloride, preferably in warm dry benzene, followed by heating until the hydrogen chloride evolution is complete. Evacuation and drying of the product, followed by crystallization, complete the process in good yields.^{4, 11, 12, 13, 28, 29} Ethyl dichlorophosphite gives the same product as phosphorus trichloride, in poorer yield.

A few selected hydroxy derivatives behave in a similar manner. Thus, N-methylol amides, upon treatment with phosphorus trichloride, form an apparently normal dichlorophosphite, ROPCl_2 , which, however, isomerizes into the phosphonyl dichloride on prolonged standing, in a reaction catalyzed somewhat by warming and by acetic anhydride. No specific phosphonyl dichlorides have been isolated in these cases; the products were hydrolyzed directly into the phosphonic acids (see Chapter 7). Hydroxymethylenecamphor reacts analogously.⁶¹ A rather interesting example of this type is displayed by diacetone alcohol.¹ This keto alcohol combines with phosphorus trichloride in a reaction that is conducted with cooling in the mixing step, followed by heating for 4 hours to 70° , to yield a cyclic ester of a phosphonyl chloride obtained many years ago by reactions discussed in Section XVII. The over-all reaction, which supposes the possibility of an enolization of the alcohol, followed by the Michaelis-Arbuzov rearrangement (common in the family of phosphite esters, but not usually observed with the halides), appears to be best represented as shown:



(Michaelis; Anschütz)

Reaction of this type throws much doubt upon the old contention that tertiary alcohols, in general, do not form phosphite esters. A considerable amount of exploration is necessary before the scope and the limitations of the reactions discussed here can be established.

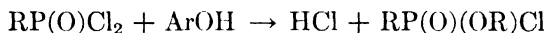
XIV. Hydrolysis of alkyl triarylmethylphosphonyl monochlorides

This rather special reaction involves the conversion of the ester chlorides of triarylmethylphosphonic acids into the corresponding monochlorides of the free acids, $\text{Ar}_3\text{CP}(\text{O})(\text{OH})\text{Cl}$. The reaction may be conducted most conveniently by warming the compounds with a solution of concentrated hydriodic acid in acetic acid.²⁸

XV. Conversion of phosphonyl dichlorides into ester chlorides

This reaction represents a semi-esterification reaction, in which only one chlorine atom of the phosphonyl dichloride is replaced by an alkoxy or aryloxy group. It is conducted by the addition of the appropriate

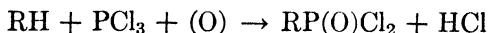
sodium alkoxide in the dry form to the phosphonyl dichloride in an inert solvent (usually benzene), followed by the filtration of the resulting sodium chloride and the isolation of the product in the usual manner.⁴ The reaction has been used mostly with the esters of the triarylmethyl series of phosphonic acids. Obviously an excess of the alkoxide results in complete esterification. Reactions of the same general type have been used more extensively with the phosphonyl dichlorides in general, when an aryl half ester was desired. In this case it is merely necessary to warm a mixture of the dihalide with an equivalent amount of the requisite phenol.⁴ (Michaelis; Hatt; Arbuzov.)



XVI. Reaction of hydrocarbons with phosphorus trichloride and oxygen

This very remarkable reaction is of very recent origin, and the possible limitations and implications have been incompletely studied. The following paragraphs contain the information available at this time.

The essence of the reaction technique is very simple. Any hydrocarbon that has at least one aliphatically bound hydrogen atom is converted to the corresponding phosphonyl dichloride upon being dissolved in phosphorus trichloride and blown with oxygen at essentially room temperature, or slightly above that. Since the reaction appears to be non-selective, all aliphatically bound hydrogens participate, and compounds with several such hydrogens, which are not in equivalent positions, yield mixtures of the appropriate isomers. Obviously only substances like cyclohexane or neopentane can yield a single isomer. The course of the reaction may be given by the rough equation



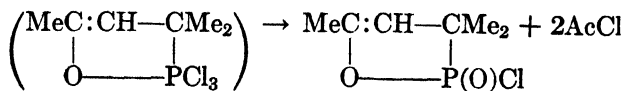
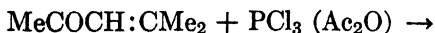
The yields appear to be best, about 25% calculated on the trichloride, when equimolar amounts of the reagents are used, with an excess of trichloride causing a slight drop in the yield. Benzene does not react, nor does phosphorus tribromide take part in the reaction. The yield is decreased by the addition of aluminum chloride, and the reaction is completely prevented by iodine or sulfuric acid (the amounts of these "negative" reagents have not been specified). The bulk of the trichloride is oxidized to phosphorus oxychloride. Light has no effect on the yield. Lower olefins form products that contain a stable chlorine, presumably formed by addition across the double bond in a manner similar to the addition of phosphorus pentachloride (see Section II).

Higher olefins (polymeric substances) do not give products with a chlorine content after mild hydrolytic treatment.¹⁴ The mechanism of this apparently general reaction is far from clear. It is, however, suggestive of the reactions of phosphines and other trivalent phosphorus compounds that take place in the presence of complex-forming reagents (see Chapters 2, 3, 6), such as aluminum chloride or sulfides. It is possible that phosphorus trichloride is activated by a termolecular collision of the three principal reagents, or that a definite reactive complex is formed between the trichloride and oxygen. (Clayton, Jensen.)

XVII. Addition of phosphorus trihalides to carbonyl compounds

Addition of halides of trivalent phosphorus derivatives to aldehydes and ketones, in the presence of suitable reagents (acetic acid, benzoic acid, acetic anhydride, water), results in the formation of hydroxy phosphonic acids, after the treatment of the products with water. Although the intermediates in such reactions are probably substances analogous to phosphoryl halides, they have not been isolated specifically. For this reason, the general topic is deferred to Chapter 7.

Ketones with unsaturation that is conjugated with the carbonyl group undergo a similar reaction and yield ketones in a reaction that may be given an over-all representation of 1,4-addition across the conjugated system. The products, thus, are keto phosphonic acids, after the hydrolytic treatment of the intermediates, when the reagent used is phosphorus trihalide or dihalide. Obviously, secondary halophosphines can yield only the corresponding keto phosphine oxides in this reaction (see Chapter 6). Until very recently the precise nature of the intermediates was largely a matter of conjecture. At the present time it is known that the intermediate in at least one specific case is truly a phosphoryl halide. The isolation of such intermediates requires conditions in which all reagents with reactive hydroxyl groups must be absent. Thus acetic anhydride is used commonly as the third reagent. The investigation of the reaction product of mesityl oxide with phosphorus trichloride in the presence of acetic anhydride gave the proved structure of the intermediate as being identical with the product discussed in Section XIII and obtained from diacetone alcohol. The reaction in the present case is



This is the first instance of definite proof of the nature of the intermediate obtained in these reactions.^{1,20} In addition, this work¹ cleared up a problem of long standing in the field of phosphorus compounds. The product shown above was obtained in 1884 by Michaelis⁵⁶ in the course of the reaction of acetone, phosphorus trichloride, and aluminum chloride. Michaelis gave a completely wrong structure of the substance, and as a matter of fact believed its trivalent phosphorus constitution in the earlier publications. It has been shown now that acetone reacts with aluminum chloride to form mesityl oxide, which then reacts as shown above.¹

Reactions of this type are conducted by mixing phosphorus trihalide (or dihalophosphine) with the unsaturated ketone and acetic anhydride and allowing the mixture to stand for several hours at 25 to 35°, after which the volatile matter is removed in vacuo and the product is isolated by vacuum distillation or ligroin extraction. (Michaelis; Anschütz; Drake, Marvel.)

XVIII. High-temperature syntheses of halophosphines

It is common to find small to moderate amounts of phosphonyl halides as by-products in the syntheses of the corresponding halophosphines. This is especially noticeable in the high-temperature reactions used in the preparation of secondary monohalophosphines, R_2PX , by such reactions as the disproportionation or the organomercury displacement, which were discussed in Chapter 3. The by-product is formed by the ordinary oxidative attack (see Section X) either by the residual air in the apparatus or by air exposure during isolation.

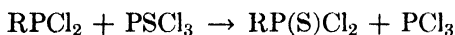
XIX. Reaction of halophosphines with sulfur

In a reaction typical of trivalent phosphorus derivatives, halophosphines add elemental sulfur to form the corresponding thionophosphonyl halides. Primary dihalophosphines require heating to above 100°, as a rule, usually in sealed tubes or in a suitable solvent. The more reactive secondary monohalophosphines react well in solutions of such low-boiling solvents as carbon disulfide.^{26,69} The products are isolated by vacuum distillation. (Guichard.)⁷²



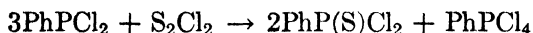
XIXA. Reaction of halophosphines with thiophosphoryl chloride. Although primary dihalophosphines accept sulfur only on rather drastic treatment (see above), the sulfur can be added in an indirect manner that yields a completely colorless product difficult to attain by

the direct element addition. Thiophosphoryl chloride is capable of transferring its sulfur atom to trivalent derivatives of phosphorus in a smooth reaction, which proceeds with phenyldichlorophosphine at a rapid rate at 115°. ²⁴ The reaction is in accord with the general order of high additive affinity of trivalent phosphorus derivative, which increases with the approach to the tertiary phosphine structure. (Gottlieb.)



XIXB. Reaction of halophosphines with sulfur monochloride.

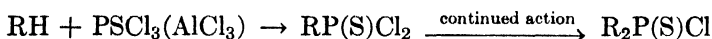
Sulfur monochloride reacts with primary dihalophosphines on moderate warming according to the following equation. ³⁷



The by-product, tetrachloride, is rather simply separated by chilling the mixture, when it separates in the form of a solid. Unless selective solvents are available, the procedure cannot be used satisfactorily with thionophosphonyl dihalides, which are solids at the usual temperatures.

XX. Friedel-Crafts reactions with thiophosphoryl chloride

Friedel-Crafts reactions of the type discussed in Chapter 3 can be performed with thiophosphoryl chloride, PSCl_3 . Although current literature discloses only one example, reaction with toluene, there is little doubt that the other aromatic substances can be engaged in this reaction. Under the general conditions given in Chapter 3, but using thiophosphoryl chloride instead of phosphorus trichloride, moderate yields of di-*p*-tolylthionophosphonyl chloride were obtained, along with smaller amounts of *p*-toluenephosphonyl dichloride, using the solvent extraction procedure. ⁵⁸ (Michaelis.)



XXI. Reaction of Grignard reagents with phosphorus oxychloride and thiophosphoryl chloride

Although phosphonyl halides have not been isolated as such from reactions of Grignard reagents with the above-mentioned reagents, there is little doubt that such substances are formed in the reactions in which a definite deficiency of the Grignard reagent is used. The reaction mixtures of this type usually give a solid insoluble precipitate, which on hydrolysis gives the corresponding acid derivatives. This solid is unquestionably a double salt or adduct of the phosphonyl halides with the by-product magnesium halide.

GENERAL CHARACTERISTICS

Compounds of the polyhalide types RPX_4 , R_2PX_3 , and R_3PX_2 are solids, which are generally poorly stable, especially those of the last type. In general they resemble phosphorus pentachloride in appearance and behavior. The substitution of two halogen atoms by such reagents as sulfur dioxide, by a semipolarly bound oxygen, has already been given in the synthetic reactions of this group; partial hydrolysis, which also produces a similar result, has also been mentioned. Complete hydrolysis, by the use of an unlimited amount of water, leads to the formation of the corresponding phosphonic acids and phosphine oxides: $\text{RP}(\text{O})(\text{OH})_2$, $\text{R}_2\text{P}(\text{O})\text{OH}$, and R_3PO , respectively. Derivatives of *p*-dialkylaminophenyl types usually undergo complete cleavage, however, under the conditions of such hydrolysis.⁶⁷ Reaction of the first two types with alcohols leads to the corresponding esters of phosphonic acids: $\text{RP}(\text{O})(\text{OR}')_2$ and $\text{R}_2\text{P}(\text{O})\text{OR}$, respectively. Reaction with amines or with amine hydrochlorides results in the formation of the corresponding phosphonamides or the quasi-phosphonium compounds of N-type, depending on conditions.

The tertiary phosphine dihalides, R_3PX_2 , vary in their stability in dependence on the radicals R. In the aromatic series, warm water treatment results in the formation of compounds of type $\text{R}_3\text{P}(\text{OH})\text{Br}$. These may be simply hydrogen-bonded adducts to the phosphoryl group, or they may be regarded as true salts. Mann inclines to the latter view, basing his view of this structure on the ionic nature of bromine, with the hydroxyl group being apparently covalently bound to the phosphorus.⁴⁵ Although all these compounds hydrolyze to the oxides in the presence of warm alkali, some of them do so on treatment with water alone.

All three types suffer thermal decomposition with the loss of one RX radical in a manner suggestive of true quaternary phosphonium halides. The reaction when carefully run is a good source of mono- and dihalophosphines.⁶⁹

The phosphonyl halides are hydrolyzed by water to the corresponding acids. The reaction is fairly slow, due undoubtedly, to some extent, to their insolubility in water. The use of alkaline solutions speeds the hydrolysis considerably. It is interesting to note that the triarylmethanephosphonyl dichlorides hydrolyze rather slowly on being boiled with water (in the presence or absence of acids or bases) to yield triarylcarbinols and phosphorous acid.⁴⁵ These can be hydrolyzed to the acids of the phosphonic type only by special methods: heating with alcoholic alkali, followed by the hydrolysis of the resulting half ester

with acetic acid and hydriodic acid.^{4, 5, 29} The thionophosphonyl halides are quite stable to water, but are rather readily hydrolyzed by alkali to the thiophosphonic acids or, to be more precise, their salts. Prolonged hydrolysis usually leads to the loss of sulfur and to the formation of the corresponding phosphonic acids.^{57, 63}

Primary phosphonyl dihalides react well with alcohols and form the corresponding dialkyl phosphonates, especially if the reaction is performed in the presence of a tertiary base or is run in vacuum at a moderately low temperature.^{73, 74} Glycols, like catechol, form the corresponding cyclic esters. Hydroquinone forms linear polymers.⁷⁶ The triarylmethanephosphonyl dichlorides again deviate from the norm. They give triarylmethane on heating with alcohol to 170 to 180° in sealed tubes,⁴ whereas sodium alkoxides can give either the chloro esters or the normal dialkyl esters, depending on the conditions used.^{28, 29}

Thionophosphonyl halides react in an interesting manner with alcoholic potassium hydrosulfide solutions. Benzenethionophosphonyl dichloride reacts with one equivalent of the reagent to form monoalkyl benzenedithiophosphonate: PhPS(OR)SH (or possibly PhP(O)(SR)SH).⁴⁴ Diphenylthionophosphonyl chloride reacts with two equivalents of the reagent to form potassium diphenyldithiophosphonate, $\text{Ph}_2\text{PS}_2\text{K}$, with evolution of hydrogen sulfide. This reaction probably proceeds via the ester, $\text{Ph}_2\text{PS(SR)}$, which is hydrolyzed by the excess hydrosulfide.⁴³

Reaction of the phosphonyl halides with amines leads to the corresponding amides of phosphonic acids; the thiono derivatives behave similarly (see Chapter 10). At elevated temperatures, under special conditions, primary amines form the imido derivatives (see Chapter 10).

Reaction of equimolar amounts of primary phosphonic acids with the corresponding phosphonyl dichlorides results in the formation of the corresponding primary metaphosphonates: RPO_2 (see Chapter 12).

Generally speaking, the polyhalides considered in this chapter retain the main reactions of phosphorus pentahalides. There is little doubt that one of the halogen atoms in these compounds is in ionic state, to all purposes, although the weight of this structure is probably less than it is in the pentahalide.⁴⁶

In a similar manner the phosphonyl halides, generally, resemble phosphorus oxychloride in their reactions. They are much less reactive and ordinarily require somewhat drastic conditions, in comparison with the polyhalides, to achieve the same end product. For this reason some doubt may be expressed about the actual formation of these substances in "over-all" hydrolysis or alcoholysis reactions of the polyhalides; such reactions usually proceed quite rapidly at gentle conditions.

ALKYL(AND ARYL)-PHOSPHORUS TETRAHALIDES

- EtPCl₄**. I.^{26, 54} Yellowish crystalline mass.
PrPCl₄. I.²⁶ Yellowish crystalline mass.
iso-PrPCl₄. I.²⁶ Yellowish crystalline mass.
iso-BuPCl₄. I.²⁶ Yellowish crystalline mass.
iso-AmPCl₄. I.^{26, 54} Yellowish crystalline mass.
Me₂C:CH·CHCl·CH₂PCl₄. II. m. 109–9.5° (from CS₂).¹²
PhPCl₄. I.^{37, 42, 51, 52, 59, 62} m. 73°. ⁵¹
PhPBr₂Cl₂. I.^{48, 51, 52} Orange, m. 208°. With excess bromine it forms PhPCl₂Br₄, m. 209°. ⁵²
PhPBr₄. I. Red mass; with excess bromine it forms PhPBr₆, a red solid that sublimes at 110°. ⁵³
4-ClC₆H₄PCl₄. I. Yellow mass. ⁵⁷
4-ClC₆H₄PCl₂Br₂. I. Red, m. 216°. ⁵⁷
4-BrC₆H₄PCl₄. I. Yellow, m. 55°. ⁵⁷
4-MeOC₆H₄PCl₄. I. Needles, m. 35–40°. ⁵⁷
4-EtOC₆H₄PCl₄. I. Needles, m. about 40°. ⁵⁷
4-PhOC₆H₄PCl₄. I. Crystalline mass. ¹⁸
4-Me₂NC₆H₄PCl₄. I. Yellow solid. ⁵⁷
4-Me₂NC₆H₄PCl₂Br₂. I. Red solid. ⁵⁷
2-MeC₆H₄PCl₄. I. Yellow m. 63–6°. ⁵⁷
3-MeC₆H₄PCl₄. I. Yellow oil, f.p. 0°. ⁵⁷
4-MeC₆H₄PCl₄. I. Yellow, m. 42°, ⁶⁵ m. 69–71°. ⁴⁰ On being heated to 100° this substance loses hydrogen chloride and the methyl group is chlorinated. ⁴⁰
2-Cl-4-MeC₆H₃PCl₄. I. Needles. ⁵⁰
4-MeC₆H₄PCl₂Br₂. I. Red, m. 128–30°. ⁴⁰
4-MeC₆H₄PBr₄. I. Red, m. 160–1°. ⁴⁰
2,5-Me₂C₆H₃PCl₄. I. m. 60°. ^{56, 78}
4-EtC₆H₄PCl₄. I. m. 51°. ⁵⁷
2,4,5-Me₃C₆H₂PCl₄. I. Greenish, m. 75°. ⁵⁷
2,4,6-Me₃C₆H₂PCl₄. I. Yellow, m. 70°. ⁵⁷
4(?) -iso-PrC₆H₄PCl₄. I. m. 53–5°. ⁵⁷
2(or 5)-Me-5(or 2)-iso-Pr·C₆H₃PCl₄. I. Oil. ⁵⁷
4-PhCH₂C₆H₄PCl₄. I. Yellow, m. 80°. ⁵⁸
4(?) -PhCH₂CH₂C₆H₄PCl₄. I. m. 65°. ⁵⁸
1-C₁₀H₇PCl₄. I.^{36, 41} m. 143°. ⁴¹
1-C₁₀H₇PCl₂Br₂. I. Orange, m. 114–6°. ⁴¹
PhC₆H₄PCl₄. I. Solid; isomer mixture. ^{42, 58}
2-Indenylphosphorus tetrachloride. II. Yellow solid. ^{4, 6}
2-Thienylphosphorus tetrachloride. I. Yellow solid. ⁷¹

COMPOUNDS OF TYPE R₂PX₃

- Ph₂PCl₃**. I. Yellow solid. ⁵⁸
(4-BrC₆H₄)PhPCl₃. I. Solid. ¹⁷
(4-MeC₆H₄)PhPCl₃. I. Yellow solid. ⁵⁸
(4-MeC₆H₄)₂PCl₃. I. Yellow solid. ⁵⁸
(2,4,5-Me₃C₆H₂)PhPCl₃. I. Yellow solid. ^{58, 58}

COMPOUNDS OF TYPE R_3PX_2

- Et_3PCl_2 . III. Crystals, dec. $240-50^\circ$.^{15, 69}
 $\text{Et}_2\text{PhPCl}_2$. I. Oil, d^{13}_4 1.216.⁶²
 $\text{Ph}_2(\text{PhCH}_2)\text{PCl}_2$. V. m. 187° .^{19, 64}
 $\text{Ph}_2(\text{PhCH}_2)\text{PClBr}$. V. m. 171° .⁴⁹
 Ph_3PCl_2 . I.³² III.²⁵ m. 176° .²⁶ In small amount, IV.³⁵
 Ph_3PBr_2 . I. Crystalline solid.⁶⁸
 $(4\text{-MeC}_6\text{H}_4)_3\text{PCl}_2$. I. Solid.⁵⁸
 $(2,4,5\text{-Me}_3\text{C}_6\text{H}_2)_3\text{PCl}_2$. I. Crystals.^{55, 58}
 $(1\text{-C}_{10}\text{H}_7)_3\text{PCl}_2$. I. Isolated as CHCl_3 complex, m. 160° .³
 $(1\text{-C}_{10}\text{H}_7)_3\text{PBr}_2$. I. Red solid.³

The following were obtained as oils by procedure I: ³¹

$\text{Pr}_2(4\text{-EtC}_6\text{H}_4)\text{PBr}_2$, $\text{Bu}_2(4\text{-EtC}_6\text{H}_4)\text{PBr}_2$, $\text{Pr}_2(4\text{-MeOC}_6\text{H}_4)\text{PBr}_2$, and
 $\text{Am}_2(4\text{-MeOC}_6\text{H}_4)\text{PBr}_2$.

PHOSPHONYL HALIDES RPOX_2 AND R_2POX

- MePOCl_2 . VI. m. 32° , b. 163° .³⁰
 EtPOCl_2 . VII.^{54, 60} VIII.²⁶ b. 175° , b_{50} $75-8^\circ$, d^{20}_4 1.1883.^{26, 54}
 $\text{ClCH}_2\text{CH}_2\text{POCl}_2$. IX at 150° from $\text{RPO}(\text{OR})_2$. $b_{5.5}$ $82-4^\circ$, b_2 68° , b. $213-7^\circ$,
 d^{16}_{10} 1.5443, d^{16}_{10} 1.5430, n^{16}_D 1.4977.^{33, 34} If the preparation (above) is conducted at
 130° , much $\text{ClCH}_2\text{CH}_2\text{POCl}(\text{OCH}_2\text{CH}_2\text{Cl})$, b_5 $123-4^\circ$, d^{22}_4 1.4528, d^{22}_{20} 1.4535,
 n^{22}_D 1.4907, is formed.³⁴
 $\text{BrCH}_2\text{CH}_2\text{POCl}_2$. IX from $\text{RPO}(\text{OR})_2$. b_{18} $119-20^\circ$, d^{20}_0 1.8262, d^{20}_4 1.8242,
 n^{20}_D 1.5210.⁷⁰
 PrPOCl_2 . VIII. b_{50} $88-90^\circ$, d^{20}_4 1.3088.²⁶
 iso-PrPOCl_2 . VIII. b_{50} $82-4^\circ$, d^{20}_4 1.3018.²⁶
 $\text{Me}(\text{CH}_2)_3\text{CPOCl}_2$. VI. b_{32} $82.5-86^\circ$, b_{30} 83° .²⁷
 iso-BuPOCl_2 . VIII. b_{50} $104-8^\circ$, d^{20}_4 1.2333.²⁶
 iso-AmPOCl_2 . VIII. b_{55} $122-5^\circ$, d^{20}_4 1.1883.²⁶
 $\text{iso-Bu}\cdot\text{CHCl}\cdot\text{POCl}_2$. VI. b_{12} $106-9^\circ$.²²
Cyclohexanephosphonyl dichloride. XVI. m. $37-7.5^\circ$, b_{15-6} $127.5-8.2^\circ$.¹⁴
 Me_2POCl . VI. m. 66° , b. 204° .³⁰
 MeEtPOCl . X. m. $37-9^\circ$, b_{15} $72-5^\circ$.⁶⁹
 Et_2POCl . VII. b_{15} $79-81^\circ$.⁶⁹
 Pr_2POCl . VII. b_{15} $112-4^\circ$.⁶⁹
 Bu_2POCl . VI.⁸⁰ VII.⁶⁹ b_{28} $156-7^\circ$, b_{15} $132-4^\circ$.⁶⁹
- $\text{MeC}:\text{CH}\cdot\text{CMe}_2\cdot\text{POCl}\cdot\text{O}$. XIII from diacetone alcohol and PCl_3 .¹ XVII from
mesityl oxide, PCl_3 and acetic anhydride,^{1, 20} or aluminum chloride (in this instance
acetone is the starting material).^{1, 56} m. $35-6^\circ$,⁵⁶ m. $31-5^\circ$,¹ b. 235° , b_{100} 154° ,⁵⁶
 b_{12} $105-6^\circ$,¹ b_{10} $100-5^\circ$,²⁰ $b_{0.01}$ 74° .¹ Addition of chlorine to the double bond
yields the dichloro derivative, m. 115° ; bromine gives the dibromo analog, m.
 142° .^{1, 56}
- PhPOCl_2 . VII.⁵¹ VI.⁵² X.^{51, 52} VIII.^{43, 51, 52, 59, 63} XI.⁷⁷ b. 258° ,⁵⁹ b_{15} $137-8^\circ$, b_4
 104° ,⁷⁷ d^{20}_4 1.375,⁵¹ d^{25}_4 1.197,⁷⁷ n^{25}_D 1.5581.⁷⁷

74 HALOPHOSPHINE HALIDES AND PHOSPHONYL HALIDES

- 4-ClC₆H₄POCl₂.** VIII.⁵⁷ XI.⁷⁷ b. 284-5°, ⁵⁷ b₃ 121-3°, ⁷⁷ d²⁰ 1.4892, ⁵⁷ d₄²⁵ 1.302, ²⁵ n_D 1.5743.⁷⁷
4-BrC₆H₄POCl₂. VIII. b. 290-1°.⁵⁷
4-MeOC₆H₄POCl₂. VIII. b. 300°, b₁₂₋₅ 173°.⁵⁷
4-EtOC₆H₄POCl₂. VIII. Oil.⁵⁷
2-MeC₆H₄POCl₂. VIII. b. 273°, d^{18.5} 1.3877.⁵⁷
3-MeC₆H₄POCl₂. VIII. b. 275°, d¹⁸ 1.3533.⁵⁷
4-MeC₆H₄POCl₂. VIII.^{50, 65} XI.⁷⁷ b. 284-5°, ^{50, 65} b₁₁ 140-2°, ⁷⁷ d₄²⁵ 1.154, ²⁵ n_D 1.5542.⁷⁷ With corresponding phenols this halide (procedure XV) yields 4-MeC₆H₄PO(OPh)Cl, m. 55°⁵⁷ and 4-MeC₆H₄PO(OC₆H₄Me-*p*)Cl, m. 60°.⁵⁷
2-Cl-4-MeC₆H₃POCl₂. VIII. m. 36°, b. 290-1°.⁶⁰
4-MeC₆H₄POBrCl. VIII. b₂₀ 160-70°.⁴⁰
4-MeC₆H₄POBr₂. VIII. m. 48-50°, b₂₀ 190°.⁴⁰
1,2-Me₂C₆H₃-x-POCl₂. VIII. Isomer mixture, m. 145°.^{57, 65}
2,5-Me₂C₆H₃POCl₂. VIII. b. 280-1°, d¹⁸ 1.31.⁷⁸
4-EtC₆H₄POCl₂. VIII. b. 294°, d¹⁶ 1.29.⁵⁷
2,4,5-Me₃C₆H₂POCl₂. VIII. b. 307-8°, m. 63°.⁵⁷
2,4,6-Me₃C₆H₂POCl₂. VIII. m. 92-3°, b. over 360°.⁵⁷
4(?) -iso-PrC₆H₄POCl₂. VIII. m. 35°, b₃₅ 183°, b. 295-300°.⁵⁷
4(?) -PhCH₂C₆H₄POCl₂. VIII. b₂₀ 261°, d²⁰ 1.207.⁵⁸
4-(PhCCl₂)C₆H₄POCl₂. VIII with PhCOC₆H₄PO₃H₂. m. 64°, b₁₅ 258°.⁵⁸
4-(PhCH₂CH₂)C₆H₄POCl₂. VIII. m. 75°.⁵⁸
(PhCH₂)₂CHPOCl₂. VIII. b₂₀ 228°, d¹⁵ 1.036.⁶¹
PhC₆H₄POCl₂. VIII. Isomer mixture, b₁₀ 220°, m. 90°.⁴²
1-C₁₀H₇POCl₂. VIII. XII. m. 60°, b₂₀ 208°.⁴¹
2-Thiophenephosphonyl dichloride. VIII. b. 258-60°.⁷¹
MePhPOCl. VI. b₁₁ 155°, b₂₂ 167°.^{23, 69}
EtPhPOCl. X. b₁₅ 207-10°.⁶⁹
Ph₂POCl. XVIII. b₁₆ 222°.^{49, 55}
(2-ClC₆H₄)₂POCl. X. b. over 340°.⁶⁹
(4-ClC₆H₄)₂POCl. X. b₂₅ 280°.⁶⁹
(4-O₂NC₆H₄)₂POCl. X. Undistillable oil.⁶⁹
(4-MeC₆H₄)PhPOCl. VII. b₂₅ 270-80°.⁵⁸
(2,4,5-Me₃C₆H₂)PhPOCl. VII. b₁₀ 210-5°.^{58, 55, 58}
(2-MeC₆H₄)₂POCl. VII.⁵⁸ X.⁶⁹ b. over 370°.^{58, 69}
(4-MeC₆H₄)₂POCl. VII.⁵⁸ X.⁶⁹ b. over 360°.^{58, 69}
(1-C₁₀H₇)₂POCl. X. Undistillable oil.⁶⁹

TRIARYLMETHANE DERIVATIVES

- Ph₃CPOCl₂.** X.²⁹ XIII.^{4, 11, 12, 13, 22, 29} m. 188-90°, ²⁹ m. 189-90°, ¹¹ m. 189.5-90°.⁴
Ph₃CPO(OH)Cl. VI.²⁹ IX.²⁹ XIII.²⁹ XIV.²⁸ m. 229-30°, ²⁹ m. 233-4°, ²⁸ Reaction with diethyl sulfate and potassium carbonate in hot xylene yields Ph₃CPO(OEt)Cl, m. 140-1°, which is also obtained from EtOPCl₂ and Ph₃COH,^{4, 29} or from Ph₃CPOCl₂ and sodium ethoxide,²⁸ or by procedure XV (in this instance the product m. 125-6°). Similarly, Ph₃CPOCl₂ in procedure XV yields the following: ⁴ Ph₃CPO(OPr-iso)Cl, m. 164-5°. Ph₃CPO(Obu-iso)Cl, m. 103-3.5°. Ph₃CPO(OMe)Cl, crude, m. 179.5-80°. Ph₃CPO(OPr)Cl, crude, m. 101°.
- (4-ClC₆H₄)Ph₂CPOCl₂.** XIII. m. 161.5°.¹²
(4-BrC₆H₄)Ph₂CPOCl₂. XIII. m. 163°.¹²
(4-MeOC₆H₄)Ph₂CPOCl₂. XIII. m. 180°.¹²

- (3-MeOC₆H₄)Ph₂CPOCl₂. XIII. m. 122-4°. ¹³
 (4-O₂NC₆H₄)Ph₂CPOCl₂. XIII. Yellow, m. 188.5°. ¹³
 (4-MeC₆H₄)Ph₂CPOCl₂. XIII. m. 193°. ¹³
 (1-C₁₀H₇)Ph₂CPOCl₂. XIII. m. 171-2°. ¹³
 (2-C₁₀H₇)Ph₂CPOCl₂. XIII. m. 194°. ¹³
 (4-PhC₆H₄)Ph₂CPOCl₂. XIII. m. 139-40°. ⁵ The product yields (4-PhC₆H₄)-Ph₂CPO(OPr-iso)Cl, m. 118-20°, by XV. ⁶
 (4-PhC₆H₄)₂PhCPOCl₂. XIII. m. 100-2°. ⁵ The product yields (4-PhC₆H₄)₂-PhCPO(OPr-iso)Cl, m. 133-4°, by XV. ⁶
 (4-PhC₆H₄)₃CPOCl₂. XIII. m. 220-2°. ⁵ The product yields by procedure XV: (4-PhC₆H₄)₃CPO(OPr)Cl, m. 139-41°, and (4-PhC₆H₄)₃CPO(OPr-iso)Cl, m. 170-3°. ⁵

DERIVATIVES WITH UNCERTAIN STRUCTURE

- (2-Oxo-3-norcamphylene)methanephosponyl dichloride. VI. Solid, m. 51°, b₁₀ 175-85°. ⁵¹

THIONOPHOSPHONYL HALIDES

- EtPSCl₂. XIX. Liquid, b₅₀ 80-2°, d²⁰ 1.3606. ²⁶
 PrPSCl₂. XIX. Liquid, b₅₀ 95-8°, d²⁰ 1.2854. ²⁶
 iso-BuPSCl₂. XIX. Liquid, b₅₀ 110-3°, d²⁰ 1.2512. ²⁶
 iso-AmPSCl₂. XIX. Liquid, b₅₀ 130-2°, d²⁰ 1.1771. ²⁶
 MeEtPSCl. XIX. Liquid, b₁₅ 96-9°. ⁶⁹
 Et₂PSCl. XIX. Liquid, b₁₅ 117-20°. ⁶⁹
 Pr₂PSCl. XIX. Liquid, b₁₅ 131-5°. ⁶⁹
 Bu₂PSCl. XIX. Liquid, b₁₅ 155-9°. ⁶⁹
 PhPSCl₂. XIX. ⁶³ XIXA. ²⁴ XIXB. ³⁷ Liquid, b. 270°, b₁₀₅ 205°, ^{27, 63} b₂₆ 150°, ²⁴ d¹³ 1.376. ⁶³
 4-MeC₆H₄PSCl₂. XX. Liquid, b₂₂₋₅ 167°. ⁵³
 MePhPSCl. XIX. Liquid, b₁₅ 140-50°. ⁶⁹
 EtPhPSCl. XIX. Liquid, b₁₅ 175-90°. ⁶⁹
 Ph₂PSCl. XIX. Liquid, b₁₅ 275-80°. ⁶⁹
 (2-ClC₆H₄)₂PSCl. XIX. Crystals, m. 41-2°. ⁶⁹
 (4-ClC₆H₄)₂PSCl. XIX. Crystals, m. 58-60°, b₁₅ 290-300°. ⁶⁹
 (4-O₂NC₆H₄)₂PSCl. XIX. Crystals, m. 172-5°. ⁶⁹
 (4-Me₂NC₆H₄)₂PSCl. XIX. Liquid, b₁₅ 270-85°. ⁶⁹
 (2-MeC₆H₄)₂PSCl. XIX. Liquid, m. 18-9°, b₁₅ 225-30°. ⁶⁹
 (4-MeC₆H₄)₂PSCl. XX. Crystals, m. 96° (from AcOH). ⁵³
 (4-MeC₆H₄)PhPSCl. XIX. Liquid, b₁₅ 265-70°. ⁶⁹
 (1-C₁₀H₇)₂PSCl. XIX. Crystals, m. 51-3°, b₁₅ 290-310°. ⁶⁹

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Quaternary Phosphonium Compounds

The substances discussed in this chapter are represented by the general formula R_4PX , where X may be a halogen or a hydroxyl (free or in the form of a salt with an acid).

METHODS OF PREPARATION

I. Addition of alkyl halides to tertiary phosphines

This simplest and most widely used process may be shown by the following equation.



The reaction is conducted by ordinary mixing of the reactants and heating. The additive affinity decreases rather rapidly with an increase of the radical size, as was pointed out in Chapter 2, where the reactivity variations of tertiary phosphines are discussed. For this reason, the compounds with the higher radicals require progressively higher temperatures, and the reactions may be conducted in sealed tubes or in suitable reflux apparatus. The lower members usually react spontaneously. The rise of reactivity of the halides from chloride through iodide is quite marked. Solvents of the polar type, such as nitromethane, may be used to stimulate the reaction. Obviously, polyhalides can react at each halogen site and form diphosphonium derivatives, etc. In the series of $ArPAlk_2$ -type phosphines, the effect of Ar substituents has been explored rather thoroughly (see Chapter 2), and it was shown that the phosphines are more reactive than the comparable arsines or amines and that the polar effect of the *m*- and *p*-substituents is less pronounced in the phosphines because of the larger bulk of the phosphorus atom.²³ A rather unusual type of phosphonium compound is obtained in such a reaction in which diaryl (*o*-methoxymethylphenethyl)phosphine is treated with hydrogen bromide in acetic acid. The cleavage of the ether link produces the corresponding *o*-bromomethyl compound, which spontaneously reacts by ring closure to form a tetrahydroisophospholinium compound.⁵¹ The products are isolated by the usual crystallizations. Under these conditions, aryl halides are essentially inert. (Hofmann; Michaelis.)

II. Reaction of tertiary phosphines with Grignard reagents or other organometallic compounds

Although tertiary phosphines, like triphenylphosphine, do not react with the Grignard reagents under the normal conditions, it has been demonstrated that a rather rapid formation of the quaternary ion takes place when such mixtures are oxygenated, that is, blown with a stream of oxygen (air may be used less effectively).^{12, 28, 33, 107} A similar reaction takes place when organolithium compounds are used, although the yields are much lower.³³ The reaction does not proceed by the way of the tertiary phosphine oxide, for the latter is inactive. Phenylsodium is ineffective.³³ The reaction most probably proceeds by the route of complex formation with the metallo-organic reagent,²⁸ a view supported by the poorer results secured with the lithium compounds, which have a lesser tendency for coordination than the magnesium derivatives.³³ This reaction may thus serve to attach an aryl group to the tertiary phosphine, a procedure impossible by direct halide addition (Section I). The isolation of the products is performed by the treatment of the crude quaternary salt, so obtained, with hydrobromic acid, which yields the phosphonium bromide derivative, or the bromide may be treated with potassium iodide to give the corresponding iodide. The final product is usually isolated by crystallization from aqueous solution.^{28, 33, 107} The use of pure tertiary phosphine is unnecessary, for we may use the crude mixture obtained by the reaction of Grignard reagents with phosphorus trihalides. A large excess of the Grignard reagent is recommended.¹⁰⁷ (Dodonov, Medoks; Gilman.)

III. Reaction of tertiary phosphines with aryl halides and aluminum chloride

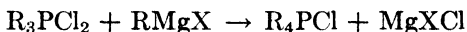
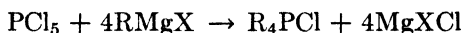
Heating triarylphosphines, specifically triphenylphosphine, with bromobenzene in the presence of aluminum chloride results in the formation of quaternary phosphonium salts, which are isolated after an aqueous treatment, to remove the aluminum, followed by conversion to a halide, usually the iodide, by conventional metathesis.¹² The above reagent pair—triphenylphosphine and bromobenzene—obviously yield the tetraphenylphosphonium ion. When the aryl group of the halide differs from that typical of the phosphine, a replacement of the latter groups takes place that is complete if an excess of the halide is used.

Thus tetraarylphosphonium ion is established readily from triphenylphosphine and an excess of bromotoluene.⁷¹ The reaction is fairly slow, requiring several hours of reflux conditions (that is, about 250 to 280°). It is believed that the reaction proceeds through the complex formation between the phosphine and aluminum chloride, a complex that had

been noted to be reactive in other respects (see Chapter 1). Too few examples of the reaction are known for a delineation of its possibilities. Obviously it cannot be used with substances that undergo degradation on heating with aluminum chloride. (Lyon, Mann.)

IV. Reaction of Grignard reagents with phosphorus halides

Reactions of this type are usually the "by-product" reactions in which a spectrum of substitution derivatives may be expected. They represent the gradual replacement of the halogen atoms in the halides in a general type of reaction, discussed in Chapters 2 and 3. The general types may be shown by the following equations, although it should be realized that products of lower degree of substitution usually accompany the desired substances.^{3, 5, 64}



Usually the reaction mixtures are quenched with water and the product isolated in the usual procedures involving metathesis to the desired negative radical. It should be noted that some quaternary compounds are also formed from trivalent phosphorus halides, under these conditions.³

V. Heating mercury phosphide with alkyl iodides

This reaction is really a variant of the metallo-organic synthesis of a tertiary phosphine, with the phosphine reacting in situ with the alkyl iodide to form the quaternary salt. The reaction gives fair yields when it is run at 130 to 160° and yields the products in the form of double salts with mercuric iodide, which is the principal by-product.⁹⁵

VI. Reaction of tertiary phosphine sulfides with alkyl halides

This reaction, which is best displayed by the alkyl iodides, such as methyl iodide, is characteristic of phosphorus compounds with a thiono group. When the sulfide is heated with an excess of the iodide to 100° or above, a progressive replacement of the aryl groups of the phosphine sulfide takes place, resulting in the eventual formation of tetra-alkyl phosphonium ion. The reaction apparently proceeds by the initial attack on the thiono group, with its eventual detachment in the form of a sulfonium ion.⁷¹ (Lyon, Mann.)

VII. Reaction of alkyl iodides with phosphorus and zinc

When mixtures of an excess of an alkyl iodide with zinc and phosphorus, or zinc phosphide, are heated in sealed tubes to 160 to 180°, appreciable amounts of the corresponding phosphonium iodides are

formed. The products are obtained as double salts with zinc iodide.^{8, 45} The establishment of the phosphonium ion is really a secondary reaction, for it represents the alkyl iodide addition to the phosphine formed in the primary reaction (see Chapter 2). (Hofmann.)

VIII. Reaction of triphenylphosphine with diphenyliodonium chloride

Refluxing a mixture of triphenylphosphine with diphenyliodonium chloride in a higher alcohol (usually propanol) results in the formation of 40 to 50% yields of tetraphenylphosphonium chloride. The use of other salts of the above iodonium compound, such as the borofluoride, gives the corresponding quaternary phosphonium salts. It is believed that the reaction proceeds by the transfer of the phenyl group as a neutral entity, rather than as an ion.⁷² The possibilities of this reaction have not been explored.

IX. Reaction of aldehydes with phosphine and hydrogen chloride

Although aldehydes do not react with phosphine under the usual conditions, a rather smooth reaction takes place when the aldehyde, in ether solution, is treated with a combined stream of hydrogen chloride and phosphine. The reaction may be regarded as an addition of phosphorus and hydrogen across the carbonyl group, activated by hydrogen chloride. The final products are quaternary phosphonium chlorides in which the 1-carbons carry a hydroxyl.



Moderate amounts of the phosphines with lesser degree of substitution usually accompany the final products (see Chapter 2).^{34, 78} It is possible to attain the same results by substitution of phosphonium iodide for the mixture of phosphine and hydrogen chloride. Aldehyde polymers may be used instead of the monomeric forms. The isolation of the products is normal, but the use of alkaline reagents is contraindicated because the products are rather readily cleaved to the initial materials. (Girard.)

X. Reaction of Grignard reagents with phosphorus sulfides

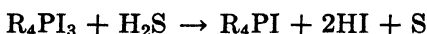
It was mentioned in Chapter 2 that tertiary phosphines are obtained in moderate yields from the reaction of Grignard reagents with phosphorus sulfides, especially those below phosphorus pentasulfide. These are accompanied by the host of products mentioned earlier, among which some quaternary phosphonium compounds are to be found. (Malatesta.)

There is little doubt that the quaternary phosphonium compounds are formed from the "primary" product mixture by the attack of the Grignard reagents (used in large excess) under the customarily drastic conditions used, temperatures of 100 to 120° for many hours. Either the phosphines or the thio derivatives may be capable of such transformations. The yields and the laborious separation of products make the reaction rather unattractive.⁷⁸

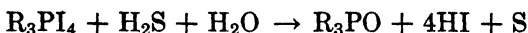
XI. Reaction of alkyl hydroxy compounds with phosphorus

Heating aliphatic alcohols with white phosphorus to high temperatures (of the order of 250°) in sealed tubes gives moderate yields (up to 20 to 30%) of quaternary phosphonium hydroxides. These may be converted to the halides for convenient isolation. This reaction, mentioned in Chapter 2, also yields a spectrum of compounds, including the phosphine series and their oxidation products. No specific study of condition variations has been made, although the starting materials are probably the most economic ones possible.⁴ (Berthaud.)

A rather similar reaction employs alkyl iodides, in which case the product mixture contains the corresponding quaternary iodides in the form of double salts with iodine. The product mixture has usually been treated with hydrogen sulfide to liberate the products, in the reaction sequence that may be partially shown by the following lines.⁷⁸

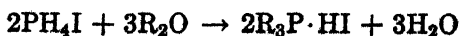
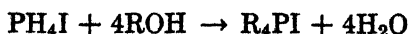
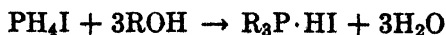


and



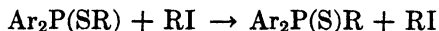
XII. Reaction of phosphonium iodide with alcohols or ethers

A somewhat smoother reaction than the one given above takes place when phosphonium iodide is heated with an excess (over 4 moles) of an alcohol to 180°. The products consist largely of the tertiary phosphine and the quaternary iodide.^{47,66} Dialkyl ethers give an even better reaction that can be conducted at lower temperatures, about 120 to 140°. ³² The usual spectrum of the lower substitution products and of their oxidation products may be expected. The equations that cover this particular case may be shown as follows.



XIII. Isomerization of alkyl diarylthiophosphinites

When the usual isomerization of alkyl diarylthiophosphinites is carried out by heating the esters with the alkyl iodides according to the general scheme shown below (see Chapter 6). (Arbuzov.)

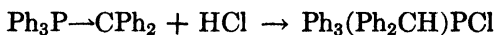


a variable amount of a phosphonium iodide of the general type $\text{Ar}_2\text{R}_2\text{PI}^1$ is formed concurrently. The origin of the phosphonium compound is not completely clear, although small amounts of the phosphines of type Ar_2RP have been isolated from these reaction mixtures that have been heated to the requisite temperatures (100 to 150°). Thus the phosphonium salts may be formed by addition of the phosphine and the alkyl iodide. The phosphine is formed probably by the attack of alkyl halide upon the sulfur, with the resulting cleavage of trialkyl-sulfonium iodide.

The products may be readily isolated by crystallization from ether, in which the main products—tertiary phosphine sulfides—are generally much more soluble than the phosphonium iodides.

XIV. Addition of hydrogen halides to phosphinemethylenes

Phosphinemethylenes, $\text{R}_3\text{P}=\text{CR}'_2$, readily add polar reagents to their semipolar bond and yield the corresponding phosphonium compounds, $\text{R}_3\text{P}(\text{X})\text{CR}'_2\text{Y}$. As a rule, this is not a very useful method for syntheses, as the starting materials are frequently made from the quaternary compounds of just this type. A representative reaction is¹⁰³



XV. Ion conversions in phosphonium compounds

The reactions listed in this section do not alter the established quaternary phosphonium ion, but merely serve to exchange a negative ion to the one of desired type. They are frequently used in the processes of isolation of the phosphonium compounds from the reaction mixtures obtained by the reactions given above.

The halides are converted to the hydroxides usually by moist silver oxide, although strong aqueous alkali has been used occasionally, particularly with the betaines.^{9, 82}

The hydroxides are converted to the halides by the appropriate acid of type HX .^{9, 16} The halides may be exchanged by treatment with the appropriate potassium or sodium halide; thus tetraphenylphosphonium bromide is converted to the chloride by a repeated crystallization from sodium chloride solution.¹⁰⁷ The same result is obtained more con-

veniently by passage of the aqueous solution over an ion-exchange resin charged with the desired halide.¹⁰⁷ The less economical methods may be listed as conversion of the iodide to the bromide by shaking with silver bromide,⁷⁶ cyanide from the iodide by treatment with silver cyanide,⁷⁰ picrate from the iodide by treatment with silver picrate,⁶² sulfate from the iodide by treatment with silver sulfate,¹⁶ nitrite from the sulfate by reaction with barium nitrite.⁹⁹

The alkoxides, which incidentally are quite unstable, have been obtained in solution by interaction of the halides with sodium alkoxides.⁴¹

It should be mentioned that the hydroxides prepared by the methods given above, from compounds in which a carbonyl group (or potential carbonyl group) is located at a site permitting a ring closure with the phosphorus atom, are essentially neutral betain-like substances.⁸² (Hofmann.)

GENERAL CHARACTERISTICS

With the exception of the hydroxides and the alkoxides, the quaternary phosphonium compounds are crystalline solids. The hydroxides are generally hygroscopic, sirupy masses, that display strongly alkaline properties, in contrast to the other members of the class, which are, in essence, salts of a strong base. Although, generally, the X group in the formulation R_4PX for the phosphonium compounds may be expected to be essentially in an ionic state, the transient existence of pentavalent phosphorus structure in such compounds has not been disproved.

One of the most useful and interesting reactions of these compounds is the decomposition that they suffer on heating (essentially dry distillation). Although the information is far from complete, for relatively few compounds have been subjected to careful study, the existing data may be summarized as follows.

Quaternary phosphonium halides decompose with formation of the tertiary phosphine, R_3P , and the organic halide, RX . The reaction may be complicated, in substances with large radicals, by the simultaneous formation of olefins, by attack on the 2-carbon.^{60,77} The predominant formation of R_3P and olefin, as reported by Collie,^{16,69} does not appear to correspond to observed facts. Obviously, quaternary halides in which not all the four radicals are identical can cleave in several ways. The work of Ingold's group,³⁰ in complement to Meisenheimer's work,⁷⁷ indicates the general order of cleavage of the various groups in the following descending order: ethyl, benzyl, methyl, propyl, isoamyl, phenyl. Since the differences between the adjacent members are not very great, appropriate mixtures may be expected.

The phosphonium hydroxides are also cleaved on heating. In this case the products are tertiary phosphine oxides, on one hand, and either paraffins or olefins (or mixtures) on the other hand. The work of Ingold's group clarified much of the earlier confusion and gave the following general order of the ease of group cleavage: benzyl, phenyl, methyl, phenethyl, ethyl, higher alkyl groups.³¹ Meisenheimer's results, however, place the phenethyl group lower in the scale, immediately after propyl, which follows ethyl.⁷⁷ The reaction of the quaternary phosphonium alkoxides is similar, but it yields more olefinic products than the decomposition of the hydroxides.^{31, 41}

The olefin or paraffin formation apparently depends upon the basicity of the ion that produces the actual decomposition. The higher basicity of the RO group serves to facilitate the olefin formation, which becomes predominant in compounds with the higher alkyl groups, and, especially, with phenethyl or 2-diphenylethyl groups.^{31, 41} Ingold's view of the process, *per se*, leans toward the establishment of a transient penta-covalent state for the phosphorus atom in these substances, followed by separation of proton, to establish the phosphoryl group, and of the alkyl ion to complete the process. It should be noted that ether formation does not take place at all in the cleavage of the alkoxides.

A form of decomposition reaction of certain phosphonium halides that is somewhat different from the above may be mentioned. Halides having at least one hydrogen on a 1-carbon can be converted into phosphinemethylenes by treatment with organolithium compounds, organosodium compounds, or alkali metals proper.^{13, 92, 103} In the compound derived from triphenylphosphine and 9-bromofluorene, this removal of hydrogen halide takes place with alcoholic ammonia.⁹⁶ (See Chapter 2.) Mention should be made of the decomposition of tetrahydroxymethylphosphonium chloride on heating with aqueous alkali. In its transformation to the corresponding tertiary phosphine oxide, the methylol group is cleaved in the form of formaldehyde and elemental hydrogen.⁴²

Unlike the derivatives of trivalent phosphorus, the aromatic members of the phosphonium compounds can be made to undergo the usual "aromatic reactions," such as nitration. Studies of this type with trimethyl-phenyl or -benzylphosphonium picrates showed that the meta orientation of the positively charged central atom decreases in the benzyl compounds (one carbon separation from the benzene ring) and substantially para-nitro derivative is formed, with some 10% of the meta isomer being estimated; the phenyl analog gives 100% yield of the meta isomer.⁵³ The effect of increases in atomic size is well displayed in the analog series of ammonium, phosphonium, and arsonium

derivatives, the greatest loss of meta orientation taking place in the large arsenic atom.⁵³

It was mentioned earlier that quaternary phosphonium halides in which a keto group, or a carboxyl, is located in a position that may give a four-membered ring, or larger, with the phosphorus atom form a special type of compounds upon conversion to the hydroxides. These compounds, which have been called phosphobetaines, may best be regarded as hydrogen-bonded or chelated substances that correspond in their general behavior to essentially neutral substances. On treatment with mineral acids, the normal quaternary salts are reformed. It may be noted that the halide obtained from triethylphosphine and ethyl chloroacetate, although behaving normally in the form of the phosphonium chloride, is decomposed to triethylphosphine oxide by the silver oxide treatment, whereas heating results in decarboxylation to methyltriethylphosphonium chloride.^{52, 100}

Phosphonium salts, as a class, form a large number of double salts, such as perhalides, as well as with salts of the heavy metals.

Quaternary phosphonium halides, being water-soluble ionic substances, have found some practical applications. Compounds based on long chain radicals possess effective surface active properties and as such have been suggested for emulsifying agents. In common with other onium salts, they appear to possess biocidal properties. However, more economical production methods must be developed to place these substances in the competitive fields.

PHOSPHONIUM COMPOUNDS

TYPE R₄PX

Me₄P-. I.⁹ IV.⁸ V.⁹⁶ VI.⁷¹ XI.⁴ XII.⁸² Hydroxide: hygroscopic sirup.^{4, 4, 9} Picrate: needles, m. over 290°.⁸¹ Iodide: crystals forming a double salt with 2HgI₂, m. 172°.^{2, 2, 9, 32, 95} and a solid periodide.³ Chloride: hygroscopic solid, yielding a double salt with mercuric chloride, m. 249°.⁹⁶ Sulfate: needles.¹⁵ Benzoate: hygroscopic solid.¹⁵ Ethoxide: unstable crystals.⁴¹

Et₄P-. I.^{9, 70} V.⁹⁶ VII.^{8, 45} XI.^{4, 75} XII.^{82, 47} Hydroxide: hygroscopic solid.^{9, 70} Ethoxide: unstable solid.⁴¹ Iodide: crystals, m. 270–8°,¹⁸ which add four atoms of chlorine or bromine; ⁷⁵ tri-iodide, m. 66–7°, is a convenient detection form for the tetraethylphosphonium ion; the iodide forms adducts or double salts with 2HgI₂, m. 117°, and with 0.5HgI₂, m. 202°.⁹⁶ Chloride: crystals, dec. 300°; ⁷⁰ readily adds chlorine.⁷⁵ Bromide: needles, dec. 320°,¹⁰⁵ which give an unstable solid adduct with six atoms of bromine.⁷⁵ Sulfate: needles.^{70, 75} Nitrite: hygroscopic solid.⁹⁰ Cyanide: hygroscopic solid.⁷⁰ Carbonate: hygroscopic solid, dec. 240°.^{2, 70} Acetate: needles, which decompose on melting.⁷⁰ Oxalate: solid, dec. 200°.⁷⁰ Benzoate: solid, m. 160°.⁷⁰

Pr₄PI. I. Crystals, dec. 200° (from EtOH).³⁰

iso-Pr₄PI. I. Cubic crystals.⁴⁸

- Bu₄P-** . I.⁶² Iodide: crystals, m. 98°. ⁶² Picrate: crystals, m. 55°. ⁶²
- iso-Bu₄PI.** I. Crystals.⁴⁸
- iso-Am₄PI.** I. Crystals.⁴⁸
- (HOCH₂)₄PCI.** IX. Needles, m. 151° (from AcOH).⁴²
- (MeCHOH)₄P-** . IX.^{34, 78} Chloride: needles, m. 112°. ⁷⁸ Bromide: crystals, m. 88°. ⁷⁸ Iodide: prisms, m. 64–5°. ³⁴ Attempted preparation of the hydroxide yields a water-soluble solid, C₈H₉O₄P. ³⁴
- (EtCHOH)₄P-** . IX.³⁴ Chloride: crystals, m. 128°. ⁷⁸ Bromide: needles, m. 105–6°. ⁷⁸ Iodide: plates, m. 95–6°. ³⁴
- (Me₂CH·CH₂CHOH)₄P-** . IX.³⁴ Iodide: crystals, m. 119°. ³⁴ Treatment with potassium hydroxide and ether yields a cleavage product: (Me₂CH·CH₂CHOH)₂-HPOH, m. 125°. ³⁴
- (n-C₆H₁₃CHOH)₄P-** . IX.³⁴ Iodide: crystals, m. 120–2°. ³⁴
- (ClCH₂)₄PCI.** By treatment of the tetramethylol analog with phosphorus pentachloride in hot carbon tetrachloride. Crystals, m. 192–3°. ⁴²
- Ph₄P-** . II.^{28, 33, 107} III.¹² IV.⁶⁴ VIII.⁷² Iodide: crystals, m. 333°, ²⁸ m. 333–43°. ¹² Bromide: crystals, m. 287°; ²⁸ dihydrate, m. 286–8°. ⁶⁴ m. 281–4°. ²⁸ Chloride: crystals, m. 265°, ²⁸ m. 265–7°. ¹⁰⁷ Nitrate: crystals, dec. 284°. ²⁸ Thiocyanate: needles, m. above 270°. ⁷¹ Sulfate: solid mass. ²⁸ Hydroxide: hygroscopic sirup. ²⁸
- (PhCH₂)₄P-** . XII.^{66, 68, 69} Iodide: needles, m. 191°. ⁶⁶ Bromide: needles, m. 216–7°. ^{66, 68, 69} Chloride: needles, m. 228.5°. ^{66, 68, 69} Nitrate: crystals. ^{66, 68, 69} Acid sulfate: crystals, m. 217°. ^{66, 68, 69} Hydroxide: plates, dec. 190°. ⁶⁸
- (3-MeC₆H₄)₄P-** . III. Iodide: crystals, m. 175–6°. ⁷¹
- (4-MeC₆H₄)₄P-** . III. Iodide: needles, m. 260–4°. ⁷¹
- (1-C₁₀H₇)₄P-** . II. Iodide: crystals, m. 270°; bromide: obtained only as a crude solid; hydroxide was obtained only in the form of solution. ⁷⁶

TYPE R₃R'PX

- Me₃EtP-** . I.⁹ Iodide: crystals. ^{9, 15} Chloride: crystals, dec. 300°. ^{15, 31} Picrate: needles, m. 290°. ³¹ Hydroxide: hygroscopic mass. ³¹
- Me₃(BrCH₂CH₂)PBr.** I. Crystals. ^{44, 100}
- Me₃(HOCH₂CH₂)P-** . I or by treatment of the above compound with silver oxide. ^{45, 52, 100} Chloride: hygroscopic solid. ^{72, 100}
- Me₃(HO₂C·CH₂)P-** . I.⁷⁹ Iodide: plates. Chloride: hygroscopic solid, which forms an orange chloroplatinate. ⁷⁹ Hydroxide: (betaine) neutral hygroscopic solid. ⁷⁹
- Me₃(EtO₂C·CH₂)P-** . I.³¹ Chloride: needles, dec. 160°. Picrate: solid, m. 124–5°. ³¹
- Me₃(EtO₂C·CHMe)PBr.** I.⁷ Crystals, m. 124–5°. ⁷
- Me₃PCH₂CH₂PM₃-** . I. Dibromide: prisms. ⁴⁵ Dichloride: forms a yellow chloroplatinate. ⁴⁵ Di-iodide: needles. ⁴⁵
- Me₃(iso-Am)P-** . I.⁹ Iodide: needles. ⁹ Chloride: forms an orange chloroplatinate. ⁹
- Me₃PhP-** . I. Iodide: crystals, m. 205°, ⁸⁰ m. 226–7°. ⁹⁷ m. 236°. ³¹ Picrate: crystals, m. 132°. ³¹ m. 132–3°. ⁵³
- Me₃(3-O₂NC₆H₄)P-** . Picrate: by nitration of the above picrate; crystals m. 166–7°. ⁵³
- Me₃(4-Me₂NC₆H₄)PI.** I. Needles, m. 264°. ⁸⁹
- Me₃(PhCH₂)P-** . I. Bromide: needles, m. 222°. ³¹ Iodide: crystals, m. 202°. ⁹⁷ Picrate: crystals, m. 173°. ⁵³

- Me₃(4-O₂NC₆H₄CH₂)P-** . I or by nitration of the above picrate.⁵⁵ Picrate: crystals, m. 188-9°.⁵³
- Me₃(3-O₂NC₆H₄CH₂)P-** . I. Picrate: crystals, m. 171-2°.⁵³
- Me₃(2-O₂NC₆H₄CH₂)P-** . I. Picrate: crystals, m. 152-3°.⁵³
- Me₃(4-MeC₆H₄)P-** . I. Iodide: needles, m. 255°.¹⁸ Chloride: crystals.¹⁸ Hydroxide: hygroscopic mass,¹⁸ which forms an orange chloroplatinate, m. 230°.¹⁸ Oxidation with potassium permanganate yields the carboxy derivative, Me₃(4-HO₂C-C₆H₄)PCl (crystals that decompose before melting); the free base of the latter (betaine) forms neutral crystals; acetate and nitrate are crystalline.¹⁸
- Me₃(2,4-Me₂C₆H₃)P-** . I. Iodide: scales, m. 265°.¹⁷ Chloride: needles, m. 110°.¹⁷ Oxidation with potassium permanganate at 55° yields Me₃(2,4-Me(HO₂C)C₆H₃)PCl: needles;¹⁷ the free betaine is a hygroscopic mass.¹⁷ Oxidation at 67-70° yields Me₃(2,4-(HO₂C)₂C₆H₃)PCl, which forms a chloroplatinate, m. 258°; treatment with silver oxide yields the free betaine, m. 160°, the silver and barium salts of which are crystalline solids (from water), while its copper salt forms insoluble needles.¹⁷
- Me₃(3,5-Me₂C₆H₃)P-** . I. Iodide: needles, m. 205°.¹⁷ Oxidation with potassium permanganate and treatment with silver oxide yields Me₃(3,5-(HO₂C)₂C₆H₃)POH, which forms the betaine, m. 115°.¹⁷
- Me₃(2,5-Me₂C₆H₃)PI.** I. Prisms, m. 204°; forms a double salt with mercuric iodide, m. 152°.⁵⁶
- Me₃(4-EtC₆H₄)PI.** I. Needles, m. 204°.⁵⁶
- Me₃(2,4,6-Me₃C₆H₂)PI.** I. Needles, m. 232°.²¹
- Me₃(4-PhOC₆H₄)PI.** I. Crystals, m. 242°.²⁵
- Et₃MeP-** . I.^{9,44,49} Iodide: plates.³¹ Chloride: crystals; forms a crystalline chloroplatinate.¹⁵ Picrate: prisms, m. 239°.³¹ Hydroxide: a hygroscopic mass.^{9,31,49}
- Et₃(ICH₂)P-** . I. Iodide: crystals.⁴¹ Chloride: forms a yellow chloroplatinate.⁴⁴
- Et₃(ClCH₂)PCl.** I. Needles; forms a yellow chloroplatinate.^{40,50}
- Me₃PCH₂CH₂PEt₃-** . I. Dibromide: crystals. Dichloride: forms a yellow chloroplatinate.⁴⁵
- Et₃PCH₂PEt₃-** . I. Dichloride: crystalline mass.⁵⁰
- Et₃PCH₂CH₂PEt₃-** I. Dibromide: needles; forms an adduct with silver bromide.⁴⁵ Dichloride: plates.⁴⁵ Di-iodide: crystals, m. 231°.⁴⁵
- Et₃(ClCH₂CH₂)PCl.** I. Needles.⁴⁵
- Et₃(BrCH₂CH₂)P-** . I. Bromide: cubes, dec. 235°.^{45,102} m. 223.¹⁰⁰ Iodide: scales.^{45,102} Chloride: needles; forms a yellow chloroaurate.^{45,102} Sulfate: needles.^{45,102} The halides, on treatment with moist silver oxide followed by aqueous silver acetate, yield Et₃(CH₂:CH)POAc.^{45,102}
- Et₃(HOCH₂CH₂)P-** . I or by treatment of the 2-chloro- or 2-bromoethyl derivative with moist silver oxide.⁴⁵ Chloride: hygroscopic mass; forms a double salt with mercuric chloride, m. 164°.⁹⁴ Bromide: isolated as the acetoxy derivative, m. 74-6°.¹⁰⁰ Iodide: needles.⁴⁵ Hydroxide: a hygroscopic mass.⁴⁵
- Et₃(H₂NCH₂CH₂)P-** . Bromide: from the 2-bromoethyl derivative on heating with alcoholic ammonia.⁴⁵ Chloride: forms a crystalline chloroaurate.⁴⁵ Hydroxide: a hygroscopic oil.⁴⁵
- Et₃(MeHNCH₂CH₂)P-** . Bromide: from the 2-bromoethyl derivative on heating with alcoholic methylamine.⁴⁵ Chloride: forms a crystalline chloroplatinate.⁴⁵
- Et₃(EtHNCH₂CH₂)P-** . Bromide: from the 2-bromoethyl derivative on heating with alcoholic ethylamine.⁴⁵ Chloride: forms an orange chloroplatinate.⁴⁵
- Et₃(Et₂NCH₂CH₂)P-** . Bromide: from the 2-bromoethyl derivative on heating with alcoholic diethylamine.⁴⁵ Chloride: forms a yellow chloroplatinate.⁴⁵

- Et₃(HO₂C·CH₂)P-** . I. Chloride: hygroscopic solid.^{46, 67} Bromide: plates.^{52, 100} Iodide: crystals.^{52, 100} Sulfate: crystals.^{52, 100} Hydroxide: obtained in solution; on drying it yields the betaine; unstable to potassium hydroxide.^{46, 67}
- Et₃(EtO₂C·CH₂)P-** . I. Chloride: a viscous hygroscopic mass,^{46, 52} which forms an orange chloroplatinate. Bromide: crystals, m. 83.2°.¹⁰⁰ Iodide: crystals.^{52, 100}
- Et₃(EtO₂C·CHMe)PBr.** I. Crystals, m. 113–4°.⁷
- Et₃((EtO)₂CH·CH₂)P-** . I. Chloride: liquid, which on heating with hydrochloric acid yields Et₃(OHC·CH₂)PCl, plates; the bromide of the latter is a crystalline solid.¹⁰
- Et₃(CH₂:CH)P-** . Bromide: by heating the 2-bromoethyl derivative to 200°.⁴⁵ Chloride and acetate form yellow chloroplatinates. Hydroxide (from the hydroxides of the 2-hydroxyethyl or 2-aminoethyl analogs on heating): a hygroscopic fluid.⁴⁵
- (Et₃P)₃CH-** . I. Tri-iodide: crystals.⁴⁸ Trichloride: forms a yellow crystalline chloroplatinate.⁴⁸
- (Et₃P)₃CCl.** I. Trichloride: a hygroscopic mass; forms a yellow chloroplatinate.⁴⁰
- (Et₃P)₃CBr.** I. Tribromide: a hygroscopic mass.⁴⁰
- (Et₃)(Me₃N(Br)CH₂CH₂)P-** . Bromide (from 2-bromoethyl derivative and trimethylamine): a hygroscopic mass.⁴⁵ Chloride: forms a crystalline chloroplatinate.⁴⁵
- Et₃PrP-** . I. Chloride: hygroscopic solid.¹⁵ Iodide: needles, m. 178–80°.^{31, 104} Picrate: crystals, m. 91°.³¹
- Et₃(BrCH₂CH₂CH₂)PBr.** I. Crystals.¹⁶
- Et₃(CH₂:CH·CH₂)PI.** I. Needles.⁴⁵
- Et₃P(CH₂)₄PEt₃-** . I. Dibromide: crystals, m. 158°.¹¹
- Et₃(iso-Am)P-** . I. Chloride and iodide are crystalline solids.^{3, 15, 49}
- Et₃(n-C₈H₁₇)PI.** I. Crystals, m. 94°.⁵⁷
- Et₃(n-C₁₀H₂₁)P-** . I. *p*-Toluenesulfonate: crystals, m. 61–5°.¹¹
- Et₃(n-C₁₂H₂₅)P-** . I. Iodide: crystals, m. 110°.⁶⁷ Perchlorate: crystals, m. 70°.¹¹
- Et₃(n-C₁₆H₃₃)PI.** I. Crystals, m. 125°.⁵⁷
- Et₃PhP-** . I. Iodide: crystals, m. 115°.^{80, 84} m. 139°.²³ Chloride: solid, m. below 100°. Bromide: crystals, m. 187–8°.²³ m. 187–9°.⁷⁷ Nitrate: crystals, m. 50–2°.⁷⁷
- Et₃(4-BrC₆H₄)PI.** I. Crystals, m. 165°.⁸¹ m. 182°.²³
- Et₃(4-MeOC₆H₄)P-** . I. Iodide: crystals, m. 65°; platinochloride, solid, m. 148°.⁸¹
- Et₃(4-PhOC₆H₄)PI.** I. Crystals, m. 181–2°.²³
- Et₃(4-Me₂NC₆H₄)PI.** I. Needles, m. 180°.⁸⁹
- Et₃(2-MeC₆H₄)PI.** I. Crystals, m. 162°.⁸¹
- Et₃(4-MeC₆H₄)PI.** I. Crystals. Platinochloride, m. 217°.¹⁹
- Et₃(PhCH₂)P-** . I. Chloride: crystals, m. 178°; chloroplatinate, solid, m. 78°.^{15, 45} Bromide: needles.¹⁴ Hydroxide: needles. Carbonate, sulfate, acetate, and oxalate are crystalline solids.¹⁴
- Et₃(PhCH₂CH₂)P-** . I. Chloride: needles. Picrate: needles, m. 70°.³¹
- Et₃(4-EtC₆H₄)PI.** I. Needles.⁸¹
- Et₃(2,4-Me₂C₆H₃)PI.** I. Crystals, m. 136°.⁸¹
- Et₃(1-C₁₀H₇)PI.** I. Crystals, m. 209°.⁸¹
- 1,2-C₆H₄(CH₂PEt₃)₂-** . I. Dibromide: crystals, m. 250°.⁹³ Di-iodide: isolated as HI salt, m. 247°.⁹³ Chlorosaurate: solid, m. 163°. Chloroplatinate: solid, m. 235–6°.⁹³
- (CH₂:CH·CH₂)₃MePI.** I. Plates, melt with decomposition.⁵⁰
- Pr₃MePI.** I. Crystals, m. 212.5°.³⁰
- Pr₃EtP-** . I. Iodide: needles, m. 124–5°. Picrate: needles, m. 64°.³¹

- Pr₃(EtO₂C·CHMe)PBr.** I. Crystals, m. 69–70°.⁷
- Pr₃BuP-** . I. Iodide: needles, m. 239–40°. ³¹ Picrate: prisms, m. 76°. ³¹
- Pr₃(n-C₈H₁₇)P-** . I. Chloride, bromide, and iodide are liquids. The chloroaurate is a solid, m. 38°. ³¹
- Pr₃PhI.** I. Crystals, m. 131.5°. ²⁶
- Pr₃(4-MeC₆H₄)PBr.** I. Needles, m. 125.5°. ²⁶
- iso-Pr₃MePI.** I. Crystals, m. above 360°. ²⁰
- Bu₃MePI.** I. Crystals, m. 133.5°. ²²
- Bu₃EtPI.** I. Crystals, m. 153°. ²²
- Bu₃PrP-** . I. Iodide: crystals. Hydroxide: a hygroscopic mass. ³¹
- Bu₃(Ph₂CH·CH₂)PCl.** I. Liquid. ³¹
- (CH₂:CMe·CH₂)₃MePI.** I. Needles, m. 151°. ⁵⁹
- (EtMeCH)₃MePI.** I. Crystals, m. 149°. ²⁰
- iso-Bu₃MePI.** I. Crystals, m. 287°. ²⁶
- iso-Am₃MePI.** I. Slowly solidifying oil. ²⁶
- Ph₃MeP-** . I. ^{86, 90} IV. ⁵ Also by heating Ph₃(EtO₂C·CH₂)PCl to 100°. ⁸⁵ Iodide: plates, m. 182–3°. ⁸⁶ m. 176–81°. ⁵ Chloride: m. 212–3°; ⁸⁶ chloroplatinate, m. 273–8°. ^{86, 90}
- Ph₃(CHI₂)PI.** I. Crystals, m. 129°. ²⁷
- Ph₃EtP-** . I. ⁹⁰ IV. ⁵ Iodide: plates, m. 164–5°. ⁹⁰ Picrate: crystals, m. 135°. ⁸⁶ Perchlorate: crystals, m. 163.5°. ⁸⁶ Nitrate: crystals, m. 127°. ⁸⁶
- Ph₃(HOCH₂CH₂)P-** . I. Chloride: crystals, m. 129–30°. ⁸⁵ Bromide: crystals, m. 114°. ⁸⁶ Iodide: crystals, m. 185–6°. ⁸⁶ Chloroplatinate: crystals, m. 222°. ⁸⁶
- Ph₃(EtO₂C·CH₂)P-** . I. Chloride: crystals, m. 90°. ⁸⁵ Bromide: crystals, m. 147°. ⁸⁶ Iodide: crystals, m. 165–6°. ⁸⁵ While silver oxide converts the product to triphenylphosphine oxide, aqueous alkali forms the free acid, which spontaneously forms the betaine, which in turn forms plates, m. 124–6°. ⁸⁶
- Ph₃PrPI.** I. Plates, m. 201.5°. ⁹⁰
- Ph₃(BrCH₂CH₂CH₂)PBr.** I. Needles, m. 226–8°. ⁸⁶
- Ph₃(Me·CO·CH₂)P-** . I. Chloride: needles, dec. 237°; ⁸⁷ chloroplatinate, m. 198°. ⁸⁷ Bromide: crystals, m. 226°. ⁸⁷ Picrate: crystals, m. 166°. ⁸⁷ Treatment with aqueous alkali yields the betaine: needles, m. 201°. ⁸⁷
- Ph₃(iso-Pr)PI.** I. Prisms, m. 191°. ⁹⁰
- Ph₃(iso-Bu)PI.** I. Needles, m. 176–7°. ⁹⁰
- Ph₃(iso-Am)PI.** I. Prisms, m. 174°. ⁹⁰
- Ph₃PCH₂PPh₃-** . I. Di-iodide: needles, dec. 230–1°. ^{86, 90}
- Ph₃PCH₂CH₂PPh₃-** . I. Dibromide: crystals, m. above 360°. ⁸⁶
- Ph₃(PhCH₂)P-** . I. Chloride: crystals, m. 287–8°. ⁹⁰ Bromide: prisms, m. 274–5°. ⁹⁰ m. 288°. ³¹ Iodide: prisms, m. 253°. ^{30, 90} Nitrate: prisms, dec. 203°. ⁹⁰ Picrate: needles, m. 148°. ⁹⁰ Dichromate: red crystals, dec. 172–4°. ⁹⁰ Thiocyanate: prisms, m. 189°. ⁹⁰
- Ph₃(Ph₂CH)PCl.** XIV. Chloride: crystals, m. 240–2°. ¹⁰³
- Ph₃(Ph·CO·CH₂)P-** . I. Bromide: crystals, m. 273–4°; ⁸⁷ m. 271–2°. ⁸⁶ Chloride: needles, m. 254–5°. ⁸⁷ Iodide: needles, m. 256–7°. ⁸⁷ Nitrate: crystals, m. 184–5°. ⁸⁷ Free betaine: crystals, m. 183–4°. ⁸⁷
- Ph₃(4-MeC₆H₄·CO·CH₂)P-** . I. Chloride: needles, m. 231°. ⁸⁷ Bromide: crystals, m. 261°. ⁸⁷ Iodide: crystals, m. 265°. ⁸⁷ Nitrate: crystals, m. 183–4°. ⁸⁷ Chloroplatinate: crystals, dec. 211°. ⁸⁷
- (4-PhOC₆H₄)₃MePI.** I. Crystals, m. 115°. ³⁶
- Triphenyl-9-fluorenylphosphonium bromide.** I. Crystals, m. 303°. ⁹⁶
- (PhCH₂)₃EtPCl.** I. Crystals, dec. 110°. ¹⁵

- (4-MeC₆H₄)₃MeP-. I. Iodide: needles, m. 108°. Chloride (dihydrate): crystals, m. 80°. Chloroplatinate: red, m. 245°. ⁸²
- (4-MeC₆H₄)₃EtPI. I. Needles, m. 185°. ⁸²
- (4-MeC₆H₄)₃(EtO₂C·CH₂)P-. I. Chloride: crystals. ⁸² Saponification with aqueous alkali yields the free betaine: solid, m. 145°. ⁸²
- (4-MeC₆H₄)₃PrPI. I. Needles, m. 182°. ⁸²
- (4-MeC₆H₄)₃(iso-Pr)PI. I. Needles, m. 184°. ⁸²
- (4-MeC₆H₄)₃(Me·CO·CH₂)P-. I. Chloride: needles, dec. 245°. Chloroplatinate: crystals, m. 220°. Bromide: crystals, dec. 210°. Iodide: crystals, m. 189°. Free betaine: needles, m. 107°. ⁸²
- (4-MeC₆H₄)₃(iso-Bu)PI. I. Crystals, m. 104°. ⁸³
- (4-MeC₆H₄)₃(Ph·CO·CH₂)P-. I. Chloride: crystals, m. 226°. Chloroplatinate: crystals, m. 240°. Bromide: crystals, m. 248°. Iodide: crystals, m. 236°. Free betaine: needles, m. 177°. ⁸²
- (2,4-Me₂C₆H₃)₃MePI. I. Crystals, m. 230.5°. ⁸³
- (2,4-Me₂C₆H₃)₃EtP-. I. Iodide: crystals, m. 225°. Chloroplatinate: crystals, m. 252°. ⁸²
- (2,5-Me₂C₆H₃)₃MePI. I. Crystals, m. 169°. ⁸²
- (2,5-Me₂C₆H₃)₃EtPI. I. Crystals, m. 220°. ⁸²
- (2,4,5-Me₃C₆H₂)₃MePI. I. Plates, m. 291°. ⁸²
- (2,4,6-Me₃C₆H₂)₃MePI. I. Crystals, m. 269°. ⁸²
- (2-PhC₆H₄)₃MePI. I. Crystals, dec. 250°. ¹⁰⁹
- (4-PhC₆H₄)₃MePI. I. Plates, dec. 135-6°. ¹⁰⁸
- (4-PhC₆H₄)₃(CH₂:CH·CH₂)PBr. I. Plates, m. 195-6°. ¹⁰⁸
- (4-PhC₆H₄)₃(EtO₂C·CH₂)P-. I. Chloride: plates, m. 164-5°. Saponification with alcoholic sodium hydroxide yields the free betaine: plates, m. 109-10°. ¹⁰⁸
- (4-PhC₆H₄)₃(PhCH₂)PBr. I. Plates, m. 277°. ¹⁰⁸

TYPE R₂R'R''PX

- Me₂(ICH₂)(4-MeC₆H₄)PI. I. Needles, m. 158-9°. ¹⁹
- Me₂EtPhPI. I. Crystals, m. 137°. ^{83, 80, 84}
- Me₂(BrCH₂CH₂)PhPBr. I. Crystals, m. 173°. ³⁵ Continued reaction yields Me₂PhP(Br)CH₂CH₂P(Br)PhMe₂, m. above 300°. ³⁵
- Me₂(BrCH₂CH₂)(4-MeC₆H₄)PBr. I. Crystals, m. 194°. ¹⁹
- Me₂Et(4-Me₂NC₆H₄)PI. I. Crystals, m. 199°. ⁸⁹
- Me₂Et(2,4,6-Me₃C₆H₂)PI. I. Crystals, m. 168°. ²¹
- Me₂(4-MeC₆H₄)(EtO₂C·CH₂)P-. I. Chloride: crystals, m. 153°. Chloroplatinate, m. 200°. ⁸²
- Me₂(4-MeC₆H₄)(HO₂C·CH₂)P-. I or saponification of the above ester with sodium carbonate. Chloride: crystals, dec. 172°. Chloroplatinate: solid, m. 220°. Free betaine: crystals, m. 206°. ⁸²
- Me₂(CH₂:CH·CH₂)PhPBr. I. Crystals, m. 113-4°. ⁷⁷
- Me₂(n-C₈H₁₇)(PhCH₂)P-. I. Chloride: oil. Iodide: solid, m. 72°. ⁸⁷
- Me₂(n-C₁₂H₂₅)(PhCH₂)P-. I. Chloride: solid, m. 176°. Iodide: solid, m. 49°. ⁸⁷
- Me₂(n-C₁₆H₃₃)(PhCH₂)P-. I. Chloride: crystals, m. 189°. Iodide: crystals, m. 66°. ⁸⁷
- Me₂Ph(PhCH₂)PCl. I. Crystals, m. 101°. ⁷⁷
- Me₂Ph(PhCH₂CH₂)PBr. I. Crystals, m. 172-2.5°. ⁷⁷
- Me₂(4-MeC₆H₄)(PhCH₂)P-. I. Chloride: oil. Chloroplatinate: solid, m. 226°. ¹⁸
- Et₂MePhPI. I. Crystals, m. 95°, ^{80, 84} m. 108-9°. ⁷⁷

- Et₂Me(4-ClC₆H₄)PI.** I. Crystals, m. 97–8°. ⁸¹
- Et₂Me(4-BrC₆H₄)PI.** I. Crystals, m. 135°. ⁸¹
- Et₂Me(4-Me₂NC₆H₄)PI.** I. Crystals, m. 186°. ⁶⁹
- Et₂Me(4-MeOC₆H₄)P-** . I. Iodide: crystals, m. 91°, ⁸¹ m. 132–3°. ²⁴ Chloroplatinate: crystals, m. 142°. ⁸¹
- Et₂Me(4-HOC₆H₄)PI.** By demethylation of the above compound. Solid, m. 168–9°. ²⁴
- Et₂Me(4-EtOC₆H₄)P-** . I. Iodide: crystals, m. 60°. Chloroplatinate: crystals, m. 208°. ⁸¹
- Et₂Me(4-PhOC₆H₄)PI.** I. Crystals, m. 163°. ²⁶
- Et₂Me(2-MeC₆H₄)PI.** I. Crystals, m. 99°. ⁸¹
- Et₂Me(4-MeC₆H₄)PI.** I. Crystals, m. 137°. ¹⁸
- Et₂Me(4-EtC₆H₄)P-** . I. Iodide: crystals, m. 135°; ⁸¹ chloroplatinate: crystals, m. 195°. ⁸¹
- Et₂Me(2,4-Me₂C₆H₃)P-** . I. Iodide: crystals, m. 90°. Chloroplatinate: crystals, m. 202°. ⁸¹
- Et₂Me(2,5-Me₂C₆H₃)P-** . I. Iodide: crystals, m. 137°, forming a salt with mercuric iodide, m. 105°. Chloroplatinate: solid, m. 137°. Tri-iodide: solid, m. 85°. ⁶⁶
- Et₂Me(2,4,5-Me₃C₆H₂)PI.** I. Crystals, m. 160°. ⁸¹
- Et₂Me(2,4,6-Me₃C₆H₂)PI.** I. Crystals, m. 125°. ⁸¹
- Et₂Me(1-C₁₀H₇)PI.** I. Crystals, m. 209°. ⁸¹
- Diethyl-methyl-2-thienylphosphonium iodide.** I. Crystals, m. 122°. ¹⁰¹
- Et₂(CH₂:CH·CH₂)PhPBr.** I. Crystals, m. 152–3°. ⁷⁷
- Et₂(EtO₂C·CH₂)(4-MeC₆H₄)P-** . I. Chloride: oil. Saponification with alkali yields the free betaine (oil), which forms a chloride, m. 96°, yielding a chloroplatinate, m. 157°. ⁸²
- Et₂(Me·CO·CH₂)(4-MeC₆H₄)P-** . I. Chloride: oil. Chloroplatinate: solid, m. 178°. Picrate: solid, m. 127°. Free betaine: crystals, m. 75°. ⁸²
- Et₂(PhCH₂)PhP-** . I. Chloride: crystals, m. 194–5°. ^{60, 77} Bromide: crystals, m. 170–1°. ⁶⁰
- Et₂(4-MeC₆H₄)(Ph·CO·CH₂)P-** . I. Chloride: oil. Chloroplatinate: crystals, m. 173°. Free betaine: crystals that liquefy in air. ⁸²
- Pr₂MePhPI.** I. Crystals, m. 137°. ²⁶
- Pr₂Me(4-MeOC₆H₄)PI.** I. Crystals, m. 60°. ⁵⁴
- Pr₂Me(4-PhOC₆H₄)PI.** I. Crystals, m. 126°. ²⁶
- Pr₂Me(4-MeC₆H₄)PI.** I. Crystals, m. 81.5°. ²⁶
- Pr₂Me(2,5-Me₂C₆H₃)P-** . I. Iodide: crystals, m. 105°, forming a double salt with mercuric iodide, m. 90°. Chloroplatinate: crystals, m. 141°. ⁶⁶
- Pr₂Me(4-EtC₆H₄)P-** . I. Iodide: oil. Chloroplatinate: crystals, m. 195°. ⁸⁴
- iso-Pr₂Me(4-PhOC₆H₄)PI.** I. Crystals, m. 203–4°. ²⁰
- Bu₂MePhPI.** I. Crystals, m. 168°. ²²
- Bu₂Me(4-MeOC₆H₄)P-** . I. Iodide: crystals, m. 86°. Chloroplatinate: crystals, m. 196°. ⁵⁴
- Bu₂Me(4-PhOC₆H₄)PI.** I. Crystals, m. 227°. ²⁶
- Bu₂Me(4-MeC₆H₄)PI.** I. Crystals, m. 130.5°. ²²
- Bu₂Me(4-EtC₆H₄)PI.** I. Oil. ⁵⁴
- Bu₂Me(2,5-Me₂C₆H₃)P-** . I. Iodide: crystals, m. 93°. Chloroplatinate: crystals, m. 215°. Tri-iodide: crystals, m. 70°. ⁶⁶
- Bu₂EtPhPI.** I. Crystals, m. 147°. ²²
- iso-Bu₂MePhPI.** I. Crystals, m. 166.5°. ²⁶

iso-Bu₂Me(4-MeC₆H₄)PI. I. Oil.²⁶

iso-Bu₂Me(2,5-Me₂C₆H₃)PI. I. Crystals, m. 120°.⁶⁶

(CH₂:CMe·CH₂)₂MePhP- . I. Iodide: crystals, m. 188°, forming a double salt with mercuric iodide, m. 133°, and with cadmium iodide, m. 114°.⁵⁹

(CH₂:CMe·CH₂)₂Me(4-MeOC₆H₄)P- . I. Iodide: crystals, m. 134.5°; forms a double salt with mercuric iodide, m. 71°, and with cadmium iodide, m. 132°.⁵⁹

(CH₂:CMe·CH₂)₂Me(4-BrC₆H₄)P- . I. Iodide: crystals, m. 174°; forms a double salt with mercuric iodide, m. 67°, and with cadmium iodide, m. 178°.⁵⁹

(CH₂:CMe·CH₂)₂Me(4-MeC₆H₄)PI. I. Crystals, m. 94°; forms a double salt with mercuric iodide, m. 79°.⁵⁹

(CH₂:CMe·CH₂)₂Me(2,5-Me₂C₆H₃)P- . I. Iodide: crystals, m. 161°; forms a double salt with mercuric iodide, m. 71°, and with cadmium iodide, m. 159°.⁵⁹

(CH₂:CMe·CH₂)₂Me(4-EtC₆H₄)PI. I. Crystals, m. 153°; forms a double salt with mercuric iodide, m. 82.5°.⁵⁹

Am₂MePhPI. I. Crystals, m. 90.5°.²⁶

Am₂Me(4-MeOC₆H₄)P- . I. Iodide: non-crystalline. Chloroplatinate: solid, m. 153°.⁵⁴

Am₂Me(4-MeC₆H₄)PI. I. Oil.²⁶

Am₂Me(2,5-Me₂C₆H₃)P- . I. Iodide: oil. Chloroplatinate: solid, m. 151°.⁵⁶

Am₂Me(4-EtC₆H₄)P- . I. Iodide: oil. Chloroplatinate: crystals.⁵⁴

iso-Am₂MePhPI. I. Crystals, m. 181.5°.²⁶

iso-Am₂Me(4-MeC₆H₄)PI. I. Crystals, m. 150°.²⁶

(MeEtCH·CH₂)₂MePhPI. I. Crystals, m. 150°.²⁶

(MeEtCH·CH₂)₂Me(4-MeC₆H₄)PI. I. Crystals, m. 131°.²⁶

(n-C₆H₁₃)₂MePhPI. I. Crystals, m. 67°.⁵⁵

(Me₂CH·CH₂·CH₂·CH₂)₂MePhPI. I. Crystals, m. 146°.²⁶

(Me₂CH·CH₂·CH₂·CH₂)₂·Me(4-MeC₆H₄)PI. I. Oil.²⁶

(Me₂CH·CH₂·CH₂·CH₂)₂EtPhPI. I. Crystals, m. 115.5°.²⁶

(n-C₇H₁₅)₂MePhPI. I. Crystals, m. 87°.⁵⁵

(n-C₈H₁₇)₂MePhPI. I. Crystals, m. 81°. Chloroplatinate: solid, m. 102°.⁵⁵

Ph₂MeEtP- . I. Iodide: crystals, m. 181°. Chloroplatinate: crystals, m. 220°.

Picrate: crystals, m. 86°.⁸⁸

Ph₂Me(CH₂:CH·CH₂)PBr. I. Crystals, m. 161°.⁷⁷

Ph₂EtPrPI. I. Crystals, m. 153-4°.⁷⁷

Ph₂Me(2-C₆H₄N)PI. I. Crystals, m. 141-2°.⁷⁴

(PhCH₂)₂MePhP- . I. Iodide: crystals, m. 206°. Nitrate: crystals, m. 162°.⁷⁷

(PhCH₂)₂EtPhPI. I. Crystals, m. 150-1°.⁷⁷

(4-Me₂NC₆H₄)₂MePhPI. I. Oil.⁸⁹

(4-Me₂NC₆H₄)₂Me(4-ClC₆H₄)P- . I. Iodide: crystals, m. 135°.⁸² Chloride (tetrahydrate): crystals, m. 72°. Chloroplatinate: crystals, dec. 235°.⁸²

(4-MeC₆H₄)₂Et(4-ClC₆H₄)PI. I. Crystals, m. 176.5°.⁸²

(4-MeC₆H₄)₂(PhCH₂)(4-ClC₆H₄)PCl. I. Dihydrate: crystals, m. 257°.⁸²

(2-C₆H₄N)₂MePhPI. I. Crystals, m. 134-5°.⁷⁴

Tri-(3-methyl-2-indolyl)-methylphosphonium iodide. I. Crystals, m. 171°.⁹¹

TYPE R₂R'₃PX

Me₂Et₂P- . I. Iodide: crystals. Chloride: hygroscopic solid.¹⁵

Me₂Ph₂P- . I.⁸⁸ XIII.¹ Iodide: needles, m. 241°.^{1, 29, 88} Chloroplatinate: yellow crystals, m. 218°.⁸⁸

Et₂Ph₂P- . I.⁸⁸ XIII.¹ Iodide: crystals, m. 204°.⁸⁸ m. 207-8°.¹ Chloroplatinate: red needles, m. 218°.⁸⁸ m. 202-3°.¹

Et₂(PhCH₂)₂PCl. I. Crystals.¹⁵

iso-Bu₂Ph₂PI. XIII. Crystals, m. 183–4°.¹

TYPE RR'R''R'''PX

MeEt(iso-Pr)(iso-Bu)PI. I. Crystals.⁴⁸

MeEtPh(4-MeOC₆H₄)PI. I. Crystals, m. 114–5°. ³⁴

MeEtPh(PhCH₂)PI. I. Crystals, m. 167–8°. ⁷⁷

MeEtPh(4-MeC₆H₄)P- . I. Iodide: crystals, m. 138°, ⁸³ m. 150°. ¹⁰⁶ *d*-Camphorsulfonate: crystals, m. 128°. ¹⁰⁶

MePrPh(4-MeOC₆H₄)PI. I. Crystals, m. 114°. ³⁴

MeEtPh(2,4,5-Me₃C₆H₂)PI. I. Oil. Chloroplatinate: solid, m. 186°. ⁸³

Me(CH₂:CH·CH₂)(4-MeC₆H₄)PhPI. I. Crystals, m. 175–7°. ^{97, 98}

MePh(PhCH₂)(4-MeC₆H₄)P- . I. Bromide: crystals, m. 211–2°. ⁹⁷ Iodide: crystals, m. 215–16°. ⁹⁷ *d*-Bromocamphorsulfonate: crystals, m. 129–31°. ⁹⁷ *d*-Camphorsulfonate: crystals, m. 134–7°. ⁹⁷

Et(CH₂:CH·CH₂)(Ph·CO·CH₂)PhPI. I. Crystals, m. 166–9°. ⁶⁰

EtPh(PhCH₂)(4-MeC₆H₄)P- . I. Iodide: crystals, m. 192°. ¹⁰⁶ Bromide: crystals, m. 215.5°. ¹⁰⁶

EtPh(PhCH₂)(Me·CO·CH₂)PCl. I. Oil. ⁶⁰

EtPh(PhCH₂)(Ph·CO·CH₂)PCl. I. Crystals, m. 166–9°. ⁶⁰

EtPh(4-MeC₆H₄)(2-BrCH₂CH₂C₆H₄CH₂)PBr. I. Crystals, m. 146–8°. ⁵¹

MePh(4-MeC₆H₄)(2-BrCH₂CH₂C₆H₄CH₂)PBr. I. Crystals, m. 185–6°. ⁵¹

MePh(4-BrC₆H₄)(2-MeOCH₂C₆H₄CH₂CH₂)PI. I. Crystals, m. 167–8°. ⁵¹

MePh(4-MeOC₆H₄)(2-MeOCH₂C₆H₄CH₂CH₂)PI. I. Crystals, m. 120.5–21°. ⁵¹

Ph(4-ClC₆H₄·CO·CH₂)(4-MeOC₆H₄)(4-MeC₆H₄)PBr. I. Crystals, m. 199°. ³⁴

CYCLIC DERIVATIVES WITH PHOSPHORUS IN THE RING

Phenyl-ethyl-tetramethylenephosphonium iodide. I. Crystals, m. 122°. ⁸⁷

Phenyl-propyl-tetramethylenephosphonium iodide. I. Crystals, m. 153–4°. ⁸⁷

Phenyl-isopropyl-tetramethylenephosphonium iodide. I. Oil. ⁸⁷

Phenyl-ethyl-pentamethylenephosphonium iodide. I. Crystals, m. 188°. ⁸⁸

***p*-Tolyl-ethyl-pentamethylenephosphonium iodide.** I. Crystals, m. 163–4°. ⁸⁸

2-Phenyl-2-(*p*-bromophenyl)-1,2,3,4-tetrahydroisophosphinolinium bromide. By simultaneous demethylation and ring closure of Ph(4-BrC₆H₄)-(2-MeOCH₂C₆H₄CH₂CH₂)P by hydrogen bromide. Crystals, m. 137–49°, remelting at 218–21°. Picrate: crystals, m. 186–7°. *d*-Camphorsulfonate: crystals, m. 206–12°. ⁵¹

2-Phenyl-2-(4-hydroxyphenyl)-1,2,3,4-tetrahydroisophosphinolinium bromide. Prepared, as above, from the 2-anisyl analog. Crystals, m. 287–87.5°; acetoxy derivative: m. 100–3°. *d*-Bromocamphorsulfonate, m. 137–47°. Camphorsulfonate: m. 174–5°, resolved into optical antipodes. ⁵¹

2-(*p*-Tolyl)-2-(*p*-chlorophenyl)-1,2,3,4-tetrahydroisophosphinolinium bromide. I. Crystals, m. 227–30°. ⁵¹

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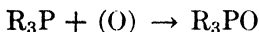
Tertiary Phosphine Oxides, Sulfides, and Selenides

Tertiary phosphine oxides, that is, compounds that consist of three radicals bound by phosphorus-carbon bonds to the phosphoryl group, are the most stable chemical structures in the family of organophosphorus compounds. As such, they may be regarded as the structural limit that is achieved or approached in the various reactions of compounds in this family. Although the corresponding sulfides and selenides hold a somewhat similar position among the sulfur- or selenium-bearing phosphorus compounds, the parallel is not exact, for these substances are readily oxidizable to the corresponding oxides.

METHODS OF PREPARATION

I. Addition of oxygen, sulfur or selenium to tertiary phosphines

One of the simplest methods of preparing tertiary phosphine oxides is the direct oxidation of the corresponding phosphines.

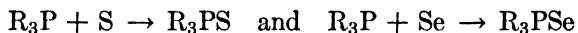


The means of such conversion of trivalent phosphorus into the phosphoryl group are numerous, as a variety of oxidizing agents are effective. However, a certain degree of selection is necessary to avoid possible side reactions. Trialkylphosphines, from the lowest to the highest reported members, are readily oxidized by exposure to air or to oxygen.^{17, 22, 25, 38, 41, 48, 59, 66, 79} Phosphines having at least one benzyl radical are also subject to such attack, whereas the aromatic phosphines are usually less subject to such mild oxidation. Thus triphenylphosphine is substantially stable in air.

Nitric acid (from 40% acid to fuming nitric acid) has long been a common laboratory reagent in such oxidations.^{7, 22, 35} Nitrous oxide is similarly effective.⁸² Potassium permanganate in aqueous solution is a very effective oxidant that may be used for rapid reactions even at room temperature for aliphatic and aromatic members, although proper precautions as to the amount of the oxidant used must be taken to avoid

oxidation of the side chains in substituted aromatic members. Chromic acid is similar in its action to the permanganate.^{28, 62, 63} The application of similarly strong oxidants, such as potassium chlorate,⁶⁸ benzoyl peroxide, or peracetic acid likewise gives nearly theoretical yields of phosphine oxides.⁷ Hydrogen peroxide,⁶⁶ mercuric oxide,⁶² and ferric chloride^{21, 67} have been useful in such oxidations at room temperature or on moderate heating. These reagents, particularly the last two, are of special interest in the oxidation of phosphines that contain substituents sensitive to oxidation, such as substituted amino groups. Benzoquinone⁸⁰ and indigo⁴⁴ have been reported to act in a similar manner. Selenium dioxide readily reacts with triphenylphosphine on being warmed, but the product of such treatment is a mixture of triphenylphosphine oxide and the corresponding selenide.⁶⁰

In a similar reaction procedure, tertiary phosphine sulfides and selenides are readily prepared by addition of the elements to the corresponding phosphines.



The reactions are ordinarily carried out in solution (ether, benzene, or carbon disulfide) on moderate warming. The reactions are usually rather exothermic, especially after an initial period of quiescence, and the addition of the element should be gradual, especially in large runs. The reaction is usually completed by reflux.^{9, 61, 63, 65, 67, 68, 76}

The indirect addition of oxygen (or sulfur) is of special interest. In these reactions organic sulfur compounds act either as sources of sulfur or as activating agents for the reagents. Thus triphenylphosphine is readily converted to the sulfide on warming in toluene solution with dibenzoyl disulfide, di-1-naphthyl disulfide, or dithiocarbamidodisulfides; dibenzyl disulfide is not effective.⁷⁸ The adduct of triethylphosphine with carbon disulfide yields triethylphosphine sulfide on prolonged standing or boiling in ether, and the same product also results from prolonged heating of the phosphine with ethyl mercaptan.⁸⁴ The reactions in which the added component serves to activate the phosphine are probably represented by the intermediate formation of a coordination complex with the phosphine. Thus triphenylphosphine is readily converted to its oxide when it is subjected to blowing with a stream of air in aqueous suspension in the presence of diphenyl disulfide. The resulting by-product, phenyl mercaptan, is reoxidized to the disulfide by the air stream, and the reaction assumes an over-all representation of oxidation of the phosphine to its oxide with a concurrent cyclic oxidation and reduction of the sulfur compound. If the air blowing is omitted, the phosphine is also oxidized to its oxide, at a slower rate, however,

with the phenyl mercaptan by-product mentioned above. In this case the oxygen is obviously supplied by water, with the disulfide again acting as an activator of the phosphorus atom.⁷⁸ In an analogous reaction, triethylphosphine is readily converted to a mixture of its oxide and sulfide upon air blowing of its solution in warm toluene in the presence of a thioketone.⁷⁹ The idea of activation of phosphorus by coordination with suitable molecules is supported by the fact that triphenylphosphine complex with aluminum chloride is easily converted to triphenylphosphine oxide by air blowing.⁸⁰

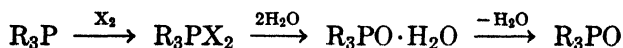
Strong oxidizing agents may be used for the conversion of tertiary phosphine sulfides, or selenides, into the corresponding oxides. Usually nitric acid or potassium permanganate are used. This procedure, ordinarily, has but little preparative significance. A modification of such direct conversion may be cited. The methiodide of triethylphosphine sulfide yields triethylphosphine oxide on long heating in water; the by-products, methyl mercaptan and hydriodic acid, indicate that the methiodide is an onium compound formed at the sulfur atom, a contention supported by conductivity data.⁸⁴

The precise mechanism of the addition of oxygen, sulfur, or selenium to the trivalent phosphorus is by no means completely known. Usually the oxidation processes are believed to proceed via the formation of a phosphine peroxide.^{25, 79} However, it is conceivable that the intermediate structures in these "addition" reactions may be more complex, involving "dimer" molecules of the phosphines linked by coordination to the addend reagent. (Hofmann; Michaelis; Schönberg.)

II. Replacement reactions of tertiary phosphine dihalides

Tertiary phosphine dihalides, R_3PX_2 , may be readily converted to the corresponding oxides by replacement reactions, among which hydrolytic reactions are most commonly used.

Such conversion may be regarded as an indirect oxidation of the phosphines, the over-all representation of which may be given as



The dihalides are as a rule rather poorly stable substances that are difficult to purify. For this reason, the actual procedures used consist of their formation and hydrolysis in situ. The halogen (bromine is commonly employed, although chlorine has been used with success⁶⁴) is added to the phosphine, either in solution in an inert solvent or in aqueous medium, and the resulting crude product is hydrolyzed by warming with water,^{18, 24, 27, 68, 85, 88} sodium hydroxide solution (the most

common procedure),^{7, 20, 57, 63, 64} or with an alcohol.²⁷ The last reagent operates, probably, through the formation of a quasi-phosphonium compound of a type $R_3P(OR)X$, which decomposes on warming in a manner common to compounds of this type. This procedure is usually widely applicable, but a notable failure should be mentioned: tri-*o*-anisylphosphine yields a tribromo derivative of its oxide, instead of the oxide proper.⁶⁴ Obviously, those compounds that suffer halogenation under mild conditions must be converted to the oxides by other methods. Other procedures for the preparation of the intermediate dihalides will be found in Chapter 4, although mention may be made of the formation of tribenzylphosphine oxide by hydrolysis of the reaction product of benzal chloride with two equivalents of phosphonium iodide; the intermediate is apparently a dihalide, R_3PI_2 .²⁷ The apparent halogen transfer between tertiary phosphines and phosphorus trichloride, in some cases, may be cited as a method of securing the intermediates. Triphenylphosphine and tri-*p*-xenylphosphine, upon being heated above 200° with phosphorus trichloride, followed by hydrolytic treatment, yield moderate amounts of the respective oxides.^{11, 88} The tri-*o*-xenyl isomer does not undergo this reaction.⁸⁹ The scope of this variant is unknown.

Addition of cyanogen bromide to triphenylphosphine, under rigorously anhydrous conditions, results in formation of an adduct that may be regarded as a form of the dihalide type. The adduct, $Ph_3P(Cn)Br$, is readily hydrolyzed to the phosphine oxide by water. If the hydrolysis is restricted, a series of intermediate products may be isolated, such as $Ph_3P(OH)_2 \cdot Ph_3P(OH)Br$ (solid, m. 141.5°) or $Ph_3P(Br)O(Br)PPh_3$ (solid, m. 140–50°).⁸⁶ These may not be true hydroxides, or dihydroxides, shown above, but rather coordination complexes with variable amounts of water. Further hydrolysis readily, and expectedly, yields triphenylphosphine oxide, although the last compound dissociates on heating in the dry state into triphenylphosphine and diphenylphosphonic acid (formed, undoubtedly, from its poorly stable phosphonyl bromide).

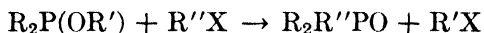
Obviously, other methods capable of conversion of a pair of phosphorus-bound halogen atoms into the phosphoryl groups should be capable of reactions considered in this section. Mention may be made of such reagents as sulfur dioxide and phosphorus pentoxide, which are well known for such replacements in the class of tetra- and trihalides. The expected by-products are thionyl halide or phosphorus oxyhalide, respectively.

The products obtained by the hydrolytic procedures are not the free phosphine oxides, but their hydrates, which are usually substances of

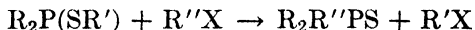
some considerable stability. The reversion to phosphine oxides may be effected, ordinarily, by heating to above 100° or by drying over suitable drying agents. In some unusual instances complete dehydration is very difficult or essentially impossible to achieve. (Michaelis.)

III. Isomerization of phosphinous and thiophosphinous acids

The reactions considered in this section are graphic illustrations of the statements made in the opening paragraph of this chapter. The main reaction scheme may be shown by the following over-all equations, which do not indicate the possible intermediate steps.^{2, 3, 6, 6b}



and



The radicals R in the original esters may be alike or different. The above reaction is merely one instance of the general Michaelis-Arbuzov rearrangement or isomerization (when $R' = R$), which is characteristic of esters based on trivalent phosphorus. The reaction is carried out by warming the mixture of the reagents to the starting temperature (usually about 100° or somewhat above), allowing the usually exothermic reaction to subside, and completing the reaction by resumed heating. The completion of the reaction may be judged either by cessation of volume change (useful in sealed tube reactions) or by cessation of distillation of the resultant halide (in open apparatus). The reaction is general for the esters of the above types and is limited in this respect only by their availability. The halide used, however, should be one in which the halogen is on an aliphatic carbon, preferably of primary type, although some tertiary halides, especially triarylmethyl halides, have been used satisfactorily. Secondary halides, as a rule, yield complex mixtures of ill-defined products. Iodides, bromides, and chlorides of hydrocarbon type, as well as acyl halides, may generally be used. Alkyl chlorides, being at the bottom of the reactivity scale, are rather sluggish in their reactions, although some especially reactive esters, such as methyl, benzyl or allyl diphenylphosphinites are readily converted to methyldiphenylphosphine oxide by methyl chloride.⁶ It should be noted that these esters suffer the "self-isomerization" to the corresponding tertiary phosphine oxides on warming with a crystal of iodine or even on strong heating, without an evident reagent. The latter property is an effective barrier to the purification of such esters by vacuum distillation. The thio analogs of the above esters are similar in their behavior.⁶

Although this reaction is customarily regarded as a sequence of addition of the halide to yield a quasi-phosphonium compound, followed by thermal decomposition,^{2,3,4} it must be realized that the true determination of the mechanism has not been performed as yet. The self-isomerization, mentioned above, is particularly difficult to explain by such a mechanism. A mechanism involving a preliminary separation of the OR' radical would appear to be more plausible. It should be noted that an attempted preparation of methyl diphenylphosphinite by the reaction of sodium methoxide with diphenylchlorophosphine results in formation of methyldiphenylphosphine oxide directly, instead of the expected ester. Although Arbuzov² regards the ester as the intermediate in this reaction, the possibility of direct oxide formation cannot be discarded on the strength of available data. This, as well as the other instances of self-isomerization cited above, deserve to be examined in detail. All the esters capable of this reaction are prepared in the presence of basic reagents (sodium alkoxides or tertiary organic bases), and there is no assurance that the resulting esters are free of traces of such bases. These have been conclusively shown to be extremely powerful catalysts of such isomerization or rearrangement reactions in the analogous syntheses of phosphonic acids.

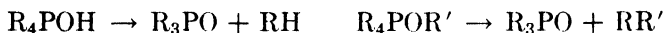
Although the reactions of the phosphinites are quite clean-cut, the reactions of their thio analogs are usually complicated by side reactions in which quaternary phosphonium halides of the type $R_2R_2''PX$ are formed. In some cases phosphines, R_2PR'' , have been isolated.³ These by-products are usually found in reaction mixtures that were heated for unduly long periods, although small amounts are found in the runs of usual duration. The formation of the phosphonium halides of the above type is readily explained by addition of the reagent halide to the phosphine, but the formation of the phosphine is not clear if the conventional Arbuzov mechanism is applied. We may assume either a preliminary separation of the SR radical of the ester or, more probably, the addition of the reagent halide to the thiophosphoryl group of the normally formed phosphine sulfide to form a sulfonium compound, which is thermally cleaved to the phosphine. Finally, the addition of the reagent halide to the divalent sulfur of the initial ester cannot be disregarded. The product of such addition may dissociate like a sulfonium compound or it may shift to a phosphonium compound, which then suffers the thermal decomposition. A study of the fate of the sulfur residue in such cases should serve to elucidate this point.

Generally speaking, the esters of phosphinous acids enter the Michaelis-Arbuzov reaction much more readily than the esters of phosphonous or phosphorous acids, thus serving to illustrate the tendency

of increased ease of such reactions as the ester approaches tertiary phosphines in its structure.^{3,6}

IV. Thermal decomposition of quaternary phosphonium compounds

Quaternary phosphonium hydroxides and alkoxides undergo thermal decomposition rather readily and form tertiary phosphine oxides, substantially according to the following equations.^{15, 17, 33, 59}



As a rule quaternary phosphonium halide is treated either with moist silver oxide^{58, 59, 88} or with strong alkali,^{35, 48, 80, 88} and the resulting hydroxide is heated in situ without further attempts at purification. If the radicals R of the quaternary compound are different from each other, the order of their separation from the phosphorus atom is of obvious importance. This is especially true if the several radicals differ only moderately in their bond strengths, for in such cases we obtain a mixture of the several possible tertiary phosphine oxides.^{59, 63} The order of elimination is given approximately (descending) by the series benzyl, phenyl, methyl, phenethyl, ethyl, higher alkyls.²⁶ Compounds containing the higher radicals usually undergo a side reaction in which olefin is eliminated, along with the hydrocarbon. This event is especially noted in the decomposition of the alkoxides, and its occurrence may be assigned, in this case, to the greater basicity of the alkoxyl in comparison with the hydroxyl ion that attacks the quaternary compound in the course of the decomposition. The phosphonium compound is given a temporarily expanded electron shell structure (10) on the central atom, which reverts to the normal configuration after the reaction.^{26, 33}

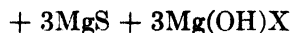
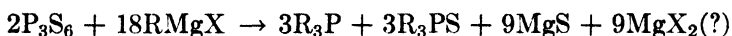
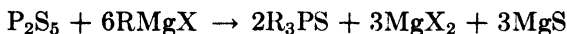
Salts of phosphonium bases, such as the nitrates, acetates, and benzoates, undergo this reaction in a similar manner.^{15, 17, 59} The quasi-phosphonium compounds of type $R_3P(OR)OH$ yield tertiary phosphine oxides in a similar manner, with elimination of ROH, whereas the related halides yield tertiary phosphine oxides on being warmed with water, probably by intermediate formation of the hydroxides.⁶⁵ It is probable that such quasi-phosphonium compounds are the intermediates in the formation of the oxides in the synthesis from phosphines via halogenation-hydrolysis (or alcoholysis) route. (Hofmann; Michaelis; Meisenheimer; Ingold.)

V. Reaction of phosphorus sulfides with Grignard reagents

Grignard reagents react at a moderate rate with the various sulfides of phosphorus and yield a host of products, the nature and the relative abundance of the constituents being dependent upon a variety of factors that are far from clear at this time.

The reaction mixtures, after the usual hydrolytic treatment, in turn yield mixtures that are composed of secondary and tertiary phosphines, tertiary phosphine sulfides and oxides, as well as thio- and dithiophosphonic acids.^{51, 52, 53} The oxygen-bearing constituents, obviously, are formed as a result of oxidative-hydrolytic attack upon the initial phosphorus-sulfur derivatives.

It must be realized that the precise structures, and even the individual existence, of some of the phosphorus sulfides are debatable. However, it may be conceded that they do represent fairly compact units in which phosphorus to sulfur bonds of essentially dicovalent sulfur are used to bind together the plurality of phosphorus atoms, which may or may not carry sulfur atoms bound by semipolar linkages. The attack of the Grignard reagent must be regarded, therefore, as a progressive cleavage of such a bond network with the eventual emergence of individual products, each carrying a single phosphorus atom. It is impossible to state categorically whether or not the addition of the Grignard reagent occurs at the semipolar or the dicovalent linkages, or whether or not a displacement in the true sense takes place. The formation of the host of products actually found by experiment, however, indicates the correctness of the "nibbling" nature of the over-all process, with the precise nature of each product being determined substantially by the laws of probability. Although we may write balanced equations for several of the products (see below), it is obviously pointless to rely upon such gross representations, especially when we realize that the yield of, say, tertiary phosphine sulfides may reach 30% of theoretical, at best.



The available information, meager as it is, indicates that the reaction should be conducted, in the present instance, with a large excess of the Grignard reagent and that the reaction mixture should be heated for several hours at 100 to 120° (usually by displacement of the original ether by toluene or a similar solvent), after which the usual hydrolytic

treatment with ammonium chloride is followed by distillation of the organic layer to recover the desired oxide. (Malatesta.)

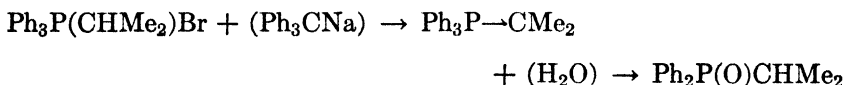
VI. Decomposition of coordination compounds of tertiary phosphines

The replacement of a group bound to the phosphorus atom of a tertiary phosphine by semipolar bond, between the phosphorus and nitrogen or carbon, by an oxygen atom can be carried out very readily by hydrolytic reactions. Such replacements may be illustrated by the representations given below for the phosphinemethylene and the phosphinimine types.^{14, 54, 82}



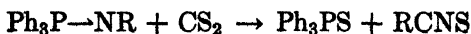
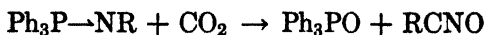
The reaction appears to be of little preparative significance because of the rather elaborate techniques needed for the formation of the necessary intermediates. The decomposition proper is performed by ordinary hydrolysis, and in many instances is spontaneous upon attack by atmospheric moisture (especially in the methylene series). The imines are usually able to form fairly stable intermediate hydrates, especially in the series of derivatives of arylsulfonamides; these, however, are converted to the phosphine oxides upon more vigorous hydrolysis.

The reaction sequence for the first category is usually conducted in situ upon formation of the intermediates. For example, the scheme for the synthesis of isopropyldiphenylphosphine oxide is shown below.



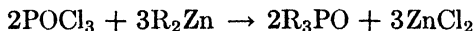
The intermediates of this type may be formed from quaternary salts, in which at least one hydrogen is available on the first carbon atom, by reaction with such reagents as triphenylmethylsodium, butyllithium, or alkali metals. The products are then treated with water.⁸³ The methylenes are also obtainable from the nitrogenous coordination compounds (Chapter 10) by thermal decomposition.

The phosphinimines are also converted to the phosphine oxides by compounds having carbonyl groups and to the phosphine sulfides by those having thiocarbonyl groups. In its simplest form, this type of decomposition is shown by the attack of carbon dioxide or disulfide.⁸² (Staudinger.)



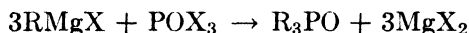
VII. Reactions of Grignard reagents with halides and esters of phosphorus acids

The precursor of this series of reactions is the reaction of dialkylzinc derivatives with phosphorus oxychloride. Treatment of such a reaction mixture with potassium hydroxide results in decomposition of zinc halide double salts and liberation of tertiary phosphine oxides.⁷²



With the advent of Grignard reagents the zinc compounds became obsolete.

Grignard reagents react in a stepwise manner with phosphorus oxyhalides, with progressive replacement of the halogen atoms by the radicals of the reagent used. Under conditions that insure an excess of the reagent (for example, by dropwise addition of phosphorus oxyhalide into the Grignard reagent) we obtain excellent yields of the tertiary phosphine oxides.^{13, 22, 38, 74, 77}



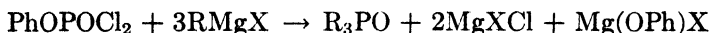
Small to moderate amounts of the products of mono- and, particularly, disubstitution may accompany the oxides. After the usual hydrolytic treatment these are isolated in the form of phosphonic acids. The yield of such products becomes substantial if the conditions specified above are not obtained (for example, reverse order of addition and use of very dilute solutions).⁴⁶ These by-products are readily separable by means of alkali, the phosphine oxides being insoluble.

Although the phosphorus oxyhalides lead to a smooth reaction, as a rule, leading in the final analysis to the tertiary products, the reaction of thio analogs is none too well known. It appears that the action of Grignard reagents, particularly those obtained from the lower alkyl halides, upon thiophosphoryl chloride (PSCl_3) results in the formation of disubstitution products only, which on hydrolytic treatment give secondary thiophosphonic acids, R_2POSH .⁸⁶ The reaction appears to stop effectively after disubstitution, and tertiary derivatives are not obtained. The point of deviation from the normally expected course, in respect to the Grignard radicals, has not been established.

Obviously, substitution of some of the halogen atoms in the oxychloride by organic radicals is not expected to change the course of the reaction, and phosphonyl halides yield tertiary phosphine oxides upon reaction with Grignard reagents. This procedure may be used for the synthesis of oxides containing different radicals R.

Chlorophosphates, that is, compounds in which one or two chlorine atoms of phosphorus oxychloride have been replaced by OR groups,

present a complex picture. Although we may expect a reaction with Grignard reagents to proceed via the substitution of the chlorine atoms by the Grignard radicals, thus leading to esters of phosphonic acids, it appears that the replacement of the OR radicals occurs with almost equal facility. In the case of phenyl dichlorophosphate, for instance, large yields of triphenylphosphine oxide result upon reaction with phenylmagnesium bromide. The reversal of the order of addition is of minor significance.⁶⁹ The total reaction is shown by:



It is unfortunate that there is no information about the effects of the relative amounts of the reagents used, the nature of the radicals, in the ester and in the Grignard reagent, and of the general conditions of the reaction. The phenoxy group in phosphates is subject to rather simple removal by a variety of other reagents and cannot be held as a typical example.

It is known that tertiary phosphate esters, $(\text{RO})_3\text{PO}$, react slowly with Grignard reagents at elevated temperatures (90° or higher) and give products of OR replacement. Thus triphenyl phosphate gives a small amount of tertiary phosphine oxides,³⁰ whereas triethyl phosphate in reacting under similar conditions with phenylmagnesium bromide yields moderate amounts of primary and secondary phosphonates, $\text{PhPO}(\text{OEt})_2$ and $\text{Ph}_2\text{PO}(\text{OEt})$.²⁹

Esters of phosphorous acid yield tertiary phosphine oxides upon being treated with Grignard reagents (or with the obsolete dialkylzinc derivatives).⁸⁷ Triethyl phosphite and phenylmagnesium bromide give a 10% yield of triphenylphosphine oxide, whereas trimethyl phosphite yields 40% of methyldiphenylphosphine oxide.²⁹ The course of the reaction is not clear, for the products may arise from oxidative attack on the products of direct substitution or from isomerization reactions of products of partial substitution, that is, esters of type $\text{R}_2\text{P}(\text{OR})$ (see Section III).

Magnesium derivatives of nitrogen heterocycles, such as indole, can be used instead of the conventional Grignard reagents. In such cases the expected tertiary phosphine oxides are accompanied by some nitrogen-phosphorus derivatives, which may be expected from the nature of these magnesium compounds.⁷⁰ (Sauvage; Pickard, Kenyon; Michaelis; Gilman.)

VIII. Heating yellow phosphorus with alkyl halides

This rather crude procedure has been reported as a source of moderate yields of tertiary phosphine oxides. The heating may be done with or

without metallic zinc. Thus ethyl iodide, zinc, and phosphorus, after being heated in a sealed tube to above 100°, followed by an aqueous treatment, give some triethylphosphine oxide. It is evident that the oxide results either from the oxidative attack upon triethylphosphine or from hydrolytic attack on the quasi-phosphonium compound (R_3PI_2) or via the decomposition route of phosphonium salts.^{20, 34, 37, 57}

IX. Reaction of dialkylanilines with phosphorus oxychloride

When phosphorus oxychloride is heated with a dialkylaniline to 130 to 140°, a progressive attack on the para position of the amine takes place. When an excess of the amine is used, the reaction is a rather clean-cut synthesis of the corresponding tertiary phosphine oxides. The by-products, primary and secondary phosphonic acids (after hydrolytic treatment), are readily separated by alkali.⁸



Phosphorus pentachloride gives the same product, probably by a route involving an intermediate of the phosphonium type.⁴⁷

The excess of the amine may be effectively replaced by a proper amount of pyridine, which then acts as acid binding agent.^{8, 46}

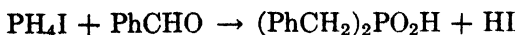
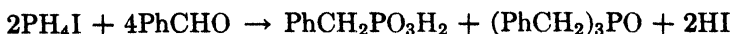
When phosphorus trichloride is used in the above reaction, a small amount of the tertiary phosphine oxide is also formed, probably by oxidative attack on the expected phosphine.⁸ (Bourneuf.)

The reaction mixture is usually freed of the excess bases by steam distillation after addition of alkali, and the tertiary phosphine oxides are isolated by taking advantage of their solubility in strong mineral acids and relative insolubility in very dilute acids.

X. Heating benzaldehyde with phosphonium iodide

Heating benzaldehyde with an excess of phosphonium iodide leads to partial substitution reactions. However, when an excess of benzaldehyde is heated in a sealed tube with phosphonium iodide to 130° for several hours and the resulting mass is subjected to an aqueous treatment, a mixture of tribenzylphosphine oxide, dibenzylphosphonic acid, and benzylphosphonic acid is formed.^{27, 49}

Although the over-all scheme has been given the form of the following equations,



it is obvious that such a set of equations is artificial. The primary products are most probably the typical aldehyde reaction products, in

which a hydroxyl group is formed on the linking carbon atom, $\text{Ph} \cdot \text{CHOH} \cdot \text{P}-$. This type of reaction is given in Chapters 2 and 5. The hydroxy derivatives are reduced by hydrogen iodide to the hydrocarbon derivatives, whereas the tertiary phosphine oxide results either by oxidative attack on the phosphine or by the thermal decomposition route of the quaternary compounds. (Litthauer.)

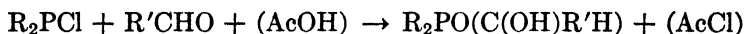
XI. Heating benzyl chloride with metal phosphides

Some tribenzylphosphine oxide is formed upon heating trisodium-phosphide with benzyl chloride and hydrolytic treatment of the product. The bulk of the product mixture is the expected tetrabenzylphosphonium chloride.¹⁷ Since the benzyl radical confers unusual oxidizability upon its derivatives with phosphorus, the oxide is evidently formed by the oxidation of the phosphine, which in turn can arise from the quaternary compound by normal thermal decomposition route.

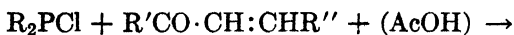
XII. Addition of secondary chlorophosphines to carbonyl compounds

This reaction is a part of a general reaction in which derivatives of trivalent phosphorus halides add to aldehydes, ketones, and unsaturated ketones to yield phosphorus derivatives. In the particular instance it has been studied only with diphenylchlorophosphine. A more detailed discussion of the general reaction is given in Chapter 7.

Diphenylchlorophosphine adds to carbonyl compounds (benzaldehyde has been the standard reagent in the study by Conant) in the presence of glacial acetic acid to give tertiary phosphine oxides in which the carbon of the original carbonyl group carries a hydroxyl.¹⁹



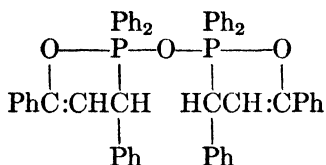
Ketones in which a double bond is conjugated with the carbonyl group undergo an essentially 1,4-addition under these conditions.



The reaction is carried out by mixing the reagents at substantially room temperature, followed by addition of acetic acid, and allowing the mixture to stand for several hours. Treatment with water and dilute alkali serves to isolate the products. The addition, curiously, is slower than the analogous addition of phosphorus trichloride or of phenyldichlorophosphine. Although a rapid addition may be expected in accord with the Arbuzov generalization concerning the approach of

structure to the phosphine type, it is evident that the bulk of the molecule is of some importance in such reactions.

In the 1,4-addition the reaction appears to proceed by way of a cyclic intermediate, which may be isolated in a crude state if pure acetic anhydride is substituted for acetic acid. The mixture of the reactants upon careful evaporation in vacuo yields a compound (or compounds) that is very sensitive to water and to acetic acid (both of which yield the corresponding phosphine oxide immediately) and that shows unsaturation by its affinity for bromine. This material has been given the provisional structure of an anhydride in which two cyclic units are bound through their phosphorus atoms by oxygen. It must be stated that the precise structure or even individuality of such a material has not been definitely established. The typical formula of such intermediate from benzalacetophenone is shown below.¹⁹



The true mechanism of the reactions in this section is not known, and the scope in respect to applicability to halophosphines, other than diphenylchlorophosphine, is similarly obscure. It is probable that the reaction is quite widely applicable. (Conant *et al.*)

GENERAL CHARACTERISTICS

Tertiary phosphine oxides are crystalline solids, usually, of a very high order of chemical stability. The notable exception must be made for benzyl derivatives, which can lose the substituent radicals on fusion with alkali, and for the esters of hydroxymethyl derivatives, which suffer a similar fate on heating with aqueous alkali.^{35,48} As it was noted earlier, the corresponding sulfides and selenides can be oxidized rather readily to the oxides.

The structures of these substances, or more precisely the nature of the bonding between the phosphorus atom and the oxygen (sulfur or selenium bonding being probably similar), have been in dispute for decades. It is an argument that covers the nature of the phosphoryl grouping in various classes of phosphorus derivatives and may be defined as an argument between the true double-bond linkage and a semipolar linkage. The "older schools" of workers in this field used the double-bond structures, and they are still used rather widely. The

main argument for them is their ability to represent the various reactions of the compounds in question as additions across a true double bond, with phosphorus atom being the more "positive" end of the linkage. The recent views on the nature of the semipolar bond appear to be more substantially logical, and one may regard the phosphoryl group in its normal state as an example of such a linkage, with the provisional possibility of an electron shift into a transient state with an expanded ten-electron shell on the atom of phosphorus. Such a provision is not unreasonable in view of the large size of this atom in comparison, for instance, with nitrogen. In addition, there is a fairly substantial body of evidence indicating the formation of substances, usually in the transient states, that call for such a reservation.

The high order of stability of the oxides makes possible a variety of substitution reactions in the constituent radicals. Such reactions, both in the aliphatic and the aromatic series, proceed normally, and in the case of the typical "aromatic" reactions lead to products that may reasonably be expected from known rules of orientation. Thus the tribenzyl derivative yields essentially pure para-trinitro derivative,¹⁰ whereas the triphenyl analog apparently yields the meta-nitro derivative exclusively.¹³ It must be added that reactions such as these should be examined on a larger scale to insure detection of the possibly minor amounts of other isomers. The oxides are unaffected by the alkali metals, although a minor extent of reduction of triethylphosphine oxide to the phosphine has been observed, apparently, in a reaction with mercury-sodium amalgam.¹⁸

Tertiary phosphine oxides form hydrates readily. These are as a rule monohydrates, although substances, like the tri-*p*-tolyl, form hemihydrates. The nature of these hydrates has been debated in a manner similar to the debate about the oxides themselves. The arguments for a dihydroxide structure and those for a hydrogen-bonded water adduct structure have not been completely conclusive for either side. Speaking for the members of the modern school, for instance, Mann in his recent survey of the problem of optical activity in the field of phosphorus compounds cited an accumulation of minor points of chemical evidence that seem to support the dihydroxide structure. Among them, the hemihydrate formation is held to have considerable weight, because of the rather doubtful probability of formation of a two-ended hydrogen bond. However, here, as in many other aspects of phosphorus chemistry, the rather conclusive evidence of physicochemical methods should be sought.

These methods, however, have not been used with great success in the class of phosphine oxides, so far as the conclusions are concerned.

Thus the dipole measurements on triphenylphosphine oxide, its hydrate, sulfide, and selenide give rather high values of 4.3–4.8 D.^{42, 73} However, this apparent solution in favor of the semipolar bond⁴² is questioned in view of the much higher values of the dipole moment in coordination compounds of the tertiary phosphines with substances like boron trichloride (7 D).⁷³ These high dipole moments are held to be evidence for the double-bond nature of the phosphoryl group, as the moment values are only slightly over 50% of the values for compounds that have the demonstrable semipolar coordinate bond.⁷³ Rather obviously, the comparison is not precise because of the nature of the bound group in the two instances. The dipole moment of the hydrate seems to be a fair argument for the hydrogen-bonded adduct. Similarly, potentiometric titrations indicate an essential lack of the conventional basicity in the oxides.⁷¹

Tertiary phosphine oxides react with phosphorus pentachloride to yield tertiary phosphine dihalides, R_3PCl_2 , in a reaction of great value, particularly among the alkyl derivatives, as a stepping stone to the good synthesis of secondary phosphine derivatives.⁷⁵

Tertiary phosphine sulfides form adducts with alkyl halides, such as methyl iodide. The adducts ionize in aqueous media and are most likely compounds of the sulfonium type. On being boiled in water they yield the tertiary phosphine oxide and methyl mercaptan (from the methyl group).³⁴

TERTIARY PHOSPHINE OXIDES

TYPE R_3PO

- Me_3PO .** I.⁹ IV.^{9, 15, 26} VII.⁷⁴ Crystals, m. 140–1°,²⁶ m. 137–8°,⁹ b. 214–5°.¹⁵ Double salts: ferrocyanide—needles; cobalticyanide—green needles; chloraurate—crystals, m. 94°; dichromate—crystals, m. 204°; chloroplatinate—crystals, m. 126°; zinc iodide—crystals, m. 168°; trichloroacetate—crystals, m. 67°.⁷⁴
- $(ClCH_2)_3PO$.** I. Crystals, m. 78°; hemihydrate: crystals, m. 88–9°.³⁵
- $(HOCH_2)_3PO$.** IV. Heated to 200° with sodium benzoate, it yields the tribenzoate: crystals, m. 110°.³⁵ Trilaurate: crystals, m. 65.5–6.5°.³⁰
- Et_3PO .** I.^{9, 82} II.^{20, 57} IV.^{16, 20, 26, 33, 57} VII.^{72, 87} VIII.⁸⁷ Hygroscopic needles, m. 50°,⁹ m. 46°,⁸² b. 238–40°,⁸² b. 243°.¹⁶ More soluble in water and alcohol than in ether; precipitated from water by potassium hydroxide.²⁵ The reported reduction to triethylphosphine by sodium has been disclaimed.^{9, 20} Double salts: cobalticyanide—crystals, m. 174°; chloraurate—crystals, m. 64–6°; dichromate—crystals, m. 100–2°; chloroplatinate—crystals, m. 150°;⁷⁴ zinc iodide—crystals, m. 99°;^{37, 81} cupric chloride—crystals, m. 233°;⁷⁴ mercuric iodide (HI salt)—crystals, m. 32–3°.⁷⁴
- Pr_3PO .** III.⁷⁵ VII.^{30, 74} Needles, m. 36°,³⁰ m. 38°,⁷⁴ m. 38–40°,⁷⁵ b. 280–2°,³⁰ b. 261–7°,⁷⁵ b. 260–5°.⁷⁴ Salt with mercuric iodide (HI salt): crystals, m. 52–4°.⁷⁴
- Bu_3PO .** I.²² III.⁷⁵ VII.²² Hygroscopic needles, b. 300°.²²
- $(CH_2: CMe \cdot CH_2)_3PO$.** I. VII. Needles, m. 132° (from Et_2O).⁴³

- Am₃PO.** I. Needles, m. 59°. ⁵⁵
- iso-Am₃PO.** I. Crystals, m. 60–5°. ³⁸
- (*n*-C₆H₁₃)₃PO.** I. Crystals. ⁴⁰
- (*n*-C₇H₁₅)₃PO.** I. Crystals. ⁴⁰
- Ph₃PO.** II. ^{7, 23, 60, 64, 68, 78} VII. ^{20, 30, 32, 46, 69, 77} The hydrolytic preparation methods yield a crystalline hydrate (dihydroxide?), which yields the oxide proper on dehydration. Plates, m. 152–3°, ⁴⁶ m. 153°, ⁶⁰ m. 153.5°, ⁷⁷ b. 360°. ⁶⁸ Soluble in sulfuric acid, but not in hydrochloric or hydriodic acids. Upon solution in fuming nitric acid, followed by dilution, this substance yields a nitrate, m. 75°, which is poorly stable in air. ⁶⁸ Salts: hydrochloride, m. 185°; chloroaurate, m. 179°; ferrocyanide, needles; zinc iodide double salt, m. 223°; cadmium iodide double salt, m. 192.5°; cobaltous chloride double salt, m. 233°; trichloroacetate, m. 97–9°. ⁷⁴
- (3-O₂NC₆H₄)₃PO.** By nitration of the above oxide with mixed acid in the cold. Yellow needles, m. 242° (from AcOH-EtOH). ^{13, 68} A by-product of unknown constitution, m. 60–8°, is also obtained.
- (3-H₂NC₆H₄)₃PO.** By reduction of the above oxide with tin and hydrochloric acid at room temperature. Plates, m. 258° (from EtOH). ^{13, 68} Triacetyl derivative, m. 186–7° (from dil. EtOH). Tribenzoyl derivative, m. 168° (from EtOH). On treatment with bromine water, the oxide forms a hexabromo derivative (probably 2,6-), crystals, dec. 205–6°. ⁶⁸
- (3-Me₂NC₆H₄)₃PO.** By heating the above oxide with methyl iodide and methanol to 100°. Needles, m. 149–52° (from EtOH). ⁶⁸ If methanol is omitted, only a tetramethyl derivative is obtained: needles, m. 182–6°. ⁶⁸
- (4-Me₂NC₆H₄)₃PO.** IX. Needles, m. 290°, ⁴⁸ m. 262°; ⁸ hydrate, m. 321° (from AcOH-EtOH). ⁸
- (4-Et₂NC₆H₄)₃PO.** IX. Needles, m. 239°. ⁴⁸
- (2-ClC₆H₄)₃PO.** II. Hemihydrate: plates, m. 226–36°. ⁵⁴
- (3-ClC₆H₄)₃PO.** II. ⁵⁴ VI. ⁵⁴ VII. ^{13, 54} Also, by diazo reaction from the amino analog. ¹³ Needles, m. 135°.
- (4-ClC₆H₄)₃PO.** VI. ⁵⁴ VII. ⁴⁶ Plates, m. 171.5–2.0°, ⁴⁶ m. 175°. ⁵⁴
- (2-MeO-3(?)-BrC₆H₃)₃PO.** II (from trianisylphosphine). Crystals, m. 245°. ⁵⁴
- (3-MeOC₆H₄)₃PO.** VI. Crystals, m. 151–2°. ⁵⁴
- (2-MeC₆H₄)₃PO.** II. VI. Hemihydrate: crystals, m. 153° (from EtOH). ⁵⁴
- (3-MeC₆H₄)₃PO.** II. Crystals, m. 111° (from ligroin). ⁵⁴
- (4-MeC₆H₄)₃PO.** II. Needles, m. 145° (from benzene). ⁶³ Forms a hemihydrate.
- (4-Me-3(?)-O₂NC₆H₃)₃PO.** By nitration of the above oxide with mixed acid. Yellow needles, m. 153° (from EtOH). ⁴³
- (4-Me-3(?)-H₂NC₆H₃)₃PO.** By reduction of the above oxide with tin and hydrochloric acid. Needles, m. 235° (from EtOH), ⁶⁸ readily soluble in hydrochloric acid.
- (4-HO₂C·C₆H₄)₃PO.** By oxidation of the tolyl derivative with chromic acid at 40–50°. Powder, m. 247°; sublimes on heating. Poorly soluble in water. ⁶⁸
- (PhCH₂)₃PO.** I. ⁴⁶ II. ²⁷ IV. ⁴⁸ VII. ^{74, 77} X. ⁴⁶ XI. ¹⁷ Needles, m. 210–2°, ¹⁷ m. 213°, ^{27, 46} m. 214°, ⁷⁴ m. 217°. ⁷⁷ Hydrochloride, m. 169°; chloroaurate, m. 222.5°. ¹⁶ Fusion with potassium hydroxide yields some dibenzylphosphonic acid. ¹⁵ Treatment with fuming sulfuric acid forms a trisulfonate. ¹⁵
- (4-O₂NC₆H₄CH₂)₃PO.** By nitration of the above with fuming nitric acid at 0°. Needles, m. 273° (from dil. AcOH), ¹⁰ m. 100°(?). ¹⁵ Pyrophoric. ¹⁰ A trace of unisolated isomer (probably ortho-) was detected in the preparation. ¹⁰
- (2,4-Me₂C₆H₃)₂PO.** II. Obtained only in crude form. ⁶³

(2,5-Me₂C₆H₃)₃PO. II. Crystals, m. 173°. ⁶³

(2,4,5-Me₃C₆H₂)₃PO. II. Prisms, m. 222° (from EtOH). ⁶³

(1-C₁₀H₇)₃PO. II.¹ VII.⁷⁷ Crystals, m. 341-2°; ¹ infusible.⁷⁷

(2-PhC₆H₄)₃PO. II. Crystals, m. 184-5° (from dil. EtOH). ⁵⁹

(4-PhC₆H₄)₃PO. II. IV. Needles, m. 233-4° (from EtOH). ⁶⁸

Tri-2-pyrrylphosphine oxide. VII. It is a poorly characterized by-product of the reaction of phosphorus oxychloride with pyrrylmagnesium.⁷⁰

Tri-2-pyridylphosphine oxide. I. Crystals, m. 209° (from EtOH). Picrate, m. 144-8° (from EtOH). ⁶⁶

Tri-3-indolylphosphine oxide. VII. Crystals, m. 138-40° (from benzene-ligroin). ⁷⁰

Tri-(2-methyl-3-indolyl)phosphine oxide. VII. Violet crystals, m. 170° (from benzene-acetone), devoid of basic properties. Forms a crystalline N-silver derivative.⁷⁰

TYPE R₃R'PO

Me₂EtPO. IV. Crystals, m. 73-5°, b. 223-5°. ²⁶

Me₂PhPO. I. IV. Crystals, m. 100°, b. 300-8°. Salt with mercuric chloride, m. 163°. ^{59, 61}

Me₂(4-Me₂NC₆H₄)PO. I. Needles, m. 62° (from Et₂O). ⁶⁷

Me₂(4-MeC₆H₄)PO. I.^{21, 62} Needles, m. 95°. ²¹

Me₂(4-HO₂C·C₆H₄)PO. By oxidation of the above oxide with dilute potassium permanganate at room temperature. Crystals, m. 240°, b. 360°. Salts: chloroplatinate, m. 234°; ammonium salt, needles, dec. 212°. Treatment with phosphorus pentachloride, followed by warming with aniline, yields the corresponding anilide, m. 235°. ⁶²

Me₂(4-Me-3(?)O₂NC₆H₃)PO. By nitration of the tolyl derivative with mixed acid. Yellow prisms, m. 175° (from EtOH). Double salt with mercuric chloride, m. 127°. ⁶³

Me₂(2,5-Me₂C₆H₃)PO. I. Needles, m. 94-5°; distillable. ⁴¹

Me₂(PhCH₂)PO. IV. Crystals, m. 58-60°, b. 303-8°. Salt with mercuric chloride, m. 115°. ⁵⁹

Et₂MePO. III.⁷⁵ IV.⁵⁹ Hygroscopic needles; sublimable. ^{59, 75}

Et₂PrPO. IV. Crude product only; m. 37°, b. 245-7°. ²⁶

Et₂PhPO. II.⁶¹ III.⁷⁵ IV.^{59, 61} Needles, m. 55-6°, b. above 360°, ⁶¹ m. 55-7°. ⁷⁵

Et₂(4-Me₂NC₆H₄)PO. I. Needles, m. 65° (from Et₂O). ⁶⁷

Et₂(4-MeC₆H₄)PO. I. Hygroscopic crystals, m. 74°. Salt with mercuric chloride, m. 135°. ⁶² Nitration with mixed acid yields an oily trinitro derivative that forms a salt with mercuric chloride, m. 105°. ⁶³

Et₂(4-HO₂C·C₆H₄)PO. By oxidation of the above oxide at room temperature with potassium permanganate. Yellow oil, distillable in vacuum. Treatment with phosphorus pentachloride, followed by warming with aniline, yields the anilide, m. 198°. ⁶²

(BrCH₂·CMeBr·CH₂)₂PhPO. II (from dimethallylphenylphosphine and bromine, followed by hydrolysis). Needles, m. 105°. ⁴³

(BrCH₂·CMeBr·CH₂)₂(4-BrC₆H₄)PO. II (similar to the above). Needles, m. 152° (from EtOH). ⁴³

(n-C₆H₁₃)₂PhPO. I. Colorless solid. ⁴⁰

(n-C₈H₁₇)₂PhPO. I. Colorless solid. ⁴⁰

Ph₂MePO. I.⁶⁶ IV.^{59, 65, 68} III.^{2, 4, 6} VI.¹⁴ VII.²⁰ Needles, m. 110°, ⁶⁶ m. 108-9°, ⁶ m. 109-10°, ^{2, 4} m. 111-2°. ⁶⁵ The product is described as the carbonate. ¹⁴

- Ph₂(Cl₃C)PO.** III. Plates, m. 137–9° (from EtOH).⁶
- Ph₂EtPO.** I.⁶⁶ III.^{2,4} IV.⁶⁸ Crystals, m. 121°.⁶⁸ m. 120.5–21°.^{2,4}
- Ph₂(Me·CO)PO.** III. Yellow prisms, m. 186–8° (from EtOH).⁶
- Ph₂(EtO₂C·CH₂)PO.** III. Crystals, m. 56–7° (from Bu₂O).⁶
- Ph₂(CH₂:CH·CH₃)PO.** III. Crystals, m. 94–5°, b₂ 200–2°.⁶
- Ph₂(Me·CO·CH₂)PO.** III. Crystals, m. 73°, b₁₀ 220–4°.⁷¹
- Ph₂(iso-Pr)PO.** III.^{2,4} VI.¹⁴ Crystals, m. 145–6°.^{2,4} m. 142–3°.¹⁴
- Ph₂(iso-Bu)PO.** III.^{2,4} Needles, m. 137.5–38°.^{2,4}
- Ph₂(iso-Am)PO.** IV. Needles, m. 96–7°.⁶⁸
- Ph₂(4-Me₂NC₆H₄)PO.** I. Colorless crystals, m. 183.5°.⁶⁷
- Ph₂(PhCH₂)PO.** II.⁶⁶ III.^{2,4,6} IV.⁶⁶ Needles, m. 192–3°.^{2,4,6} m. 195–6°.⁶⁶ On treatment with mixed acid this oxide forms a trinitro derivative, m. 206°.²⁴
- Ph₂(3-HO₂C·C₆H₄)PO.** I (from *m*-tolylidiphenylphosphine with potassium permanganate). Crystals, m. 232°.²⁸
- Ph₂(4-MeC₆H₄)PO.** II. Crystals, m. 129–30° (from EtOH).²⁴
- Ph₂(Ph·CHOH)PO.** XII. Crystals, m. 230°.¹⁹
- Ph₂(Ph₃C)PO.** III. Crystals, m. 227.5–28°.⁶ m. 227–9° (from EtOH).⁶
- Ph₂(Ph·CO·CH₂·CHPh)PO.** XII (from benzalacetophenone). Crystals, m. 227° (from EtOH).¹⁹ Bromination in boiling chloroform yields Ph₂(Ph·CO·CHBr·CHPh)PO, m. 187°, which on boiling with methanolic potassium acetate reverts in part to the initial phosphine oxide. Alcoholic sodium hydroxide, however, yields the expected unsaturated oxide: Ph₂(Ph·CO·CH:CPh)PO, m. 143°, which does not add bromine. If the bromination is performed with the original reaction mixture (prepared with acetic anhydride, instead of acetic acid), the products include not only the above bromo derivative but also its lower-melting isomer, m. 158°, which is readily reduced to Ph₂(Ph·CO·CH₂·CHPh)PO with zinc and acetic acid.¹⁹
- Ph₂(4-ClC₆H₄·CO·CH₂·CHPh)PO.** XII (from benzal-*p*-chloroacetophenone). Crystals, m. 225–6°.¹⁹ Bromination of this oxide in boiling chloroform yields Ph₂(4-ClC₆H₄·CO·CHBr·CHPh)PO, m. 187°, which on boiling with alcoholic sodium hydroxide yields the original oxide. If the bromination is performed with the original reaction mixture (made with acetic anhydride), the products include not only the above bromo derivative but also its higher-melting isomer, m. 196°, which on heating with alcoholic alkali yields only the unsaturated oxide: Ph₂(4-ClC₆H₄·CO·CH:CPh)PO, m. 151°.¹⁹
- (PhCH₂)₂PhPO.** I. Needles, m. 174° (from EtOH).⁶⁰
- (4-MeC₆H₄)₂MePO.** IV. Crystals, m. 143° (from EtOH).⁶³
- (4-MeC₆H₄)₂(4-ClC₆H₄)PO.** II. Needles, m. 130°.⁶³ Oxidation with chromic acid yields the dicarboxylic acid (plates) which is poorly soluble in water.⁶³
- (4-PhC₆H₄)₂MePO.** IV (from R₃MePI). Needles, m. 223–4° (from EtOH).⁶⁸
- (4-PhC₆H₄)₂(CH₂:CH·CH₂)PO.** IV. Crystals, m. 192–3° (from dil. EtOH).⁸⁸

TYPE RR'R'PO

- MeEtPhPO.** III.⁷⁶ IV. Colorless crystals, m. 50–2°.⁷⁶ m. 50°, b. above 360°.^{88,89}
- The bromocamphorsulfonate has been partially resolved.^{88,89}
- MePrPhPO.** IV. Needles, m. 158°; monohydrate: oil; b₁₈ 180°.⁶⁰
- EtPrPhPO.** IV. Plates, m. 44–5°, b₁₅ 184–5°.⁶⁰
- MePh(4-Me₂NC₆H₄)PO.** IV. Crystals, m. 146°.⁶⁷
- MePh(PhCH₂)PO.** IV. Crystals, m. 148–9°, b₁₅ 235°.⁶⁰ The camphorsulfonate has been resolved; *d*-camphorsulfonate of the *l*-form, m. 94°; *l*-camphorsulfonate of the *d*-form, m. 111°. [α]_D²⁰ 73° (in HCl).⁶⁰

EtPh(PhCH₂)PO. I. IV. Crystals, m. 110–1°. ⁵⁹

BuPh(4-Ph·CO·OC₆H₄)PO. I. Crystals, m. 136° (from dil. EtOH). ²³

TERTIARY PHOSPHINE SULFIDES

TYPE R₃PS

Me₃PS. I. ⁹ V. ⁵¹ Prisms, m. 105° (from water). ^{9, 51}

Et₃PS. I. ^{9, 36, 81, 84} V. ⁵³ Crystals, m. 94° ^{9, 53}; soluble in water and distillable with steam. Its methiodide, m. 123°, ³⁴ forms an adduct with two molecules of iodoform, which melts at 84°. ⁸⁴

(iso-Bu)₃PS. V. Crystals, m. 59–60°. ⁵¹

(iso-Am)₃PS. I. Crystals, m. 95.5–6.5°. ⁸²

Ph₃PS. I. ^{12, 84, 88, 78} V. ⁵³ VII. ⁸⁶ Needles, m. 157.5°, ⁶⁸ m. 158°, ⁵³ m. 161° (from EtOH), ⁸⁶ b. above 360°. ⁶⁸

(PhCH₂)₃PS. I. ⁴⁸ VII. ⁸⁶ Needles, m. 266°, ⁴⁸ m. 274° (from CHCl₃). ⁸⁶

(4-MeC₆H₄)₃PS. I. Needles, m. 182° (from EtOH). ⁶³

(2,4-Me₂C₆H₃)₃PS. I. Plates, m. 167°. ⁶³

(2,5-Me₂C₆H₃)₃PS. I. Crystals, m. 170°. ⁶³

(2,4,6-Me₃C₆H₂)₃PS. I. Plates, m. 192° (from EtOH). ⁶³

(4-PhC₆H₄)₃PS. I. Plates, m. 241–2°. ⁸³

Tri-2-pyridylphosphine sulfide. I. Crystals, m. 161° (from EtOH). Picrate, m. 156–8°; methiodide, m. 156–7°. ⁸⁶

TYPE R₂R'PS

Me₂(4-Me₂NC₆H₄)PS. I. Crystals, m. 155° (from EtOH). ⁶⁷

Et₂PhPS. I. Oil, freezing to needles in freezing mixture; b. over 360°. ⁸¹

Et₂(4-Me₂NC₆H₄)PS. I. Crystals, m. 148°. ⁶⁷

Et₂(PhCH₂)PS. I. Crystals, m. 94–5°, b. 300–10°. ¹⁶

Ph₂EtPS. III. Plates, m. 65.5–66°. ^{3, 4}

Ph₂PrPS. III. Plates, m. 97–8°. ^{3, 4}

Ph₂(CH₂:CH·CH₂)PS. III. Crystals, m. 49–50°, b. 184–5°. ⁶

Ph₂(iso-Bu)PS. III. Rhombic crystals, m. 80–1°. ^{3, 4}

Ph₂(iso-Am)PS. III. Rhombic crystals, m. 63.5°, b. 230–40°. ^{3, 4}

Ph₂(4-Me₂NC₆H₄)PS. I. Needles, m. 183°. ⁶⁷

Ph₂(PhCH₂)PS. III. Crystals, m. 144–7°. ⁶

Ph₂(2-C₆H₄N)PS. I. Crystals, m. 119° (from EtOH). ⁵⁶

(4-MeC₆H₄)₂(4-ClC₆H₄)PS. I. Crystals, m. 149°. ⁶³

(2-C₆H₄N)₂PhPS. I. Crystals, m. 141° (from EtOH). Dihydrochloride, m. 165–71°. Picrate, m. 141.5–2.5°. ⁵⁶

TYPE RR'R'PS

EtPh(4-HOC₆H₄)PS. I. Crystals, m. 83–4° (from EtOH). ²³

EtPh(4-HO₂C·CH₂OC₆H₄)PS. By heating the sodium derivative of the above compound with ethyl bromoacetate and hydrolyzing the resulting ester with aqueous sodium hydroxide. Crystals, m. 84° (from benzene-cyclohexane). *l*-Phenylethylamine salt, m. 206–7°. *d*-*sec*-Butylamine salt, m. 189–90°. ²³

BuPh(4-Ph·CO·OC₆H₄)PS. I. Crystals, m. 66–7° (from EtOH). ²³

BuPh(4-HOC₆H₄)PS. By hydrolysis of the above compound with sodium hydroxide solution. Crystals, m. 97–8° (from cyclohexane). ²³

BuPh(4-HO₂C·CH₂OC₆H₄)PS. By heating the above compound with ethyl bromoacetate in alcoholic sodium ethoxide, followed by saponification with aqueous sodium hydroxide. A solid, insoluble in water.²³ Its phenylethylamine salt, m. 209–10°, was resolved into optical isomers. The free acid has: $[M]_D = 9.6^\circ$.²³

Ph(4-BrC₆H₄)(4-Me₂NC₆H₄)PS. I. Crystals, m. 126° (from MeOH).²³ N-methiodide(?) (must be made in nitromethane solution or without solvent), m. 158–9°. N-metho-*d*-camphorsulfonate, m. 224–6°. N-methobromocamphorsulfonate, m. 198°.²³

Ph(4-MeOC₆H₄)(4-MeC₆H₄)PS. I. Crystals, m. 121–4° (from EtOH).²³

Ph(4-BrC₆H₄)(2-C₆H₄N)PS. I. Crystals, m. 109° (from EtOH).²³ Methiodide (made in nitromethane at 50°), yellow solid, m. 132–4°.²³

Ph(4-BrC₆H₄)(3-C₆H₄N)PS. I. Crystals, m. 115–6° (from EtOH).²³ Does not form a methiodide.²³

TERTIARY PHOSPHINE SELENIDES

TYPE R₃PSe

Me₃PSe. I.^{9,76} Needles, m. 140°,⁷⁶ m. 84° (crude).⁹

Et₃PSe. I.^{9,86} Prisms, m. 112°.

Ph₃PSe. I.^{60,68} Needles, m. 184–5°,⁶⁰ m. 184–6° (from EtOH).⁶⁸

(PhCH₂)₃PSe. I. Needles, m. 256–5° (from AcOH).⁴⁸

(4-MeC₆H₄)₃PSe. I. Needles, m. 193° (from EtOH).⁶⁸

TYPE R₂R'PSe

(4-MeC₆H₄)₂(4-ClC₆H₄)PSe. I. Needles, m. 172°.⁶³

TYPE RR'R''PSe

Ph(4-BrC₆H₄)(4-Me₂NC₆H₄)PSe. I. Crystals, m. 135.5–6.5°.²³

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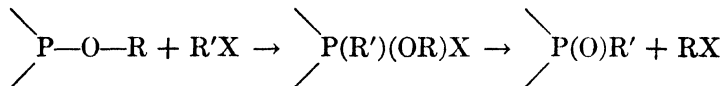
***Phosphinous, Phosphonous,
and Phosphonic Acids,
Their Sulfur Analogs and Esters***

The compounds described in this chapter are substances that possess one or two organic radicals bound directly to the central phosphorus atom, the residual valences of which are constituting an acid function or an ester based on such acid function. The general types of substances considered in this category may be listed as primary and secondary phosphonic acids [$\text{RP}(\text{O})(\text{OH})_2$ and $\text{R}_2\text{P}(\text{O})\text{OH}$], phosphonous acids (RPO_2H_2), phosphinous acids (R_2POH), the thio analogs of the above substances in which one or more oxygen atoms in the above formulas are replaced by sulfur, including primary and secondary thiophosphinous acids (RHPSH and R_2PSH), and the esters of all the above-listed acids, in which one or more "acidic" hydrogen atoms are replaced by organic radicals.

METHODS OF PREPARATION

I. Reactions of derivatives of trivalent phosphorus

IA. Reaction of tertiary phosphites with organic halides. The most general formulation of this reaction, which is best termed the Michaelis-Arbuzov reaction, may be given as follows:



The reaction in this form takes place with any derivative of trivalent phosphorus that carries an ester group OR, and a most varied selection of the organic halides $\text{R}'\text{X}$ are able to participate in the reaction. Although customarily used with tertiary phosphites $(\text{RO})_3\text{P}$ when the reaction product is an ester of a primary phosphonic acid, $\text{RP}(\text{O})(\text{OR})_2$, the reaction may be used with esters of phosphonous acids ($\text{RP}(\text{OR})_2$) to form esters of secondary phosphonic acids ($\text{R}_2\text{P}(\text{O})\text{OR}'$), esters of phosphinous acids (R_2POR) to form tertiary phosphine oxides (see Chapter 6), and esters of the thio analogs of the oxygen acids to form

the similar products in the sulfur series. If the radical R' is identical with the radical R of the ester group, the reaction takes on the aspects of a true isomerization, which can be performed with minute amounts of the halide $R'X$. (Michaelis, Kähne; Arbuzov.)

The chief requirement of the structure of the organic halide is that the halogen atom must be on the terminal atom, that is, it must not be directly connected to an aromatic ring. Generally, primary aliphatically bound halides are most satisfactory reagents. Secondary aliphatic halides tend to give side reactions, such as dehydrohalogenation or Würtz-like twinning of the radical R' . Tertiary halides have been studied but little; it is known, however, that triarylmethyl halides react normally. Acyl halides react satisfactorily to yield the corresponding keto-phosphonates (or acylphosphonates). Organic polyhalides are capable of multiple reaction, the above reaction scheme taking place at each halogen atom.¹

The principal failures among the organic halides have been given for the following types. Halides with a nitro group do not react normally, although the primary addition step appears to take place. The final products, however, are abnormal and largely unknown; usually tertiary phosphates appear among the products, indicating an over-all oxidation of the tertiary phosphites. Secondary halides react satisfactorily only with esters of phosphonous or phosphinous acids; the reaction with phosphites, which are much less reactive, ordinarily does not take place or leads to olefin formation.⁸⁸

The reaction proper is conducted by mixing the reactants and warming the mixture to the required temperature, most often about 150° . The usual reactivity scale of iodide-bromide-chloride applies to this reaction, as does the general principle of decreasing reactivity with the growth of molecular size in any particular class. The reactivity of the ester reagents increases rapidly from the phosphites to the phosphonites and, eventually, to the phosphinites, in accord with the generally increased reactivity upon approach to the tertiary phosphine structure.^{5, 6, 88, 242} The most reactive combinations enter the reaction at room temperature; this is especially true of reactions with acyl halides.¹¹¹ If the radicals R' and R are different, it is advisable to remove the resulting halide RX as rapidly as possible in order to prevent its interaction with any unreacted trivalent phosphorus ester.¹³⁵ If the halide $R'X$ contains more than one halogen atom it is necessary to use a large excess of the halide to reduce the polysubstitution reaction to minor proportions.¹⁸⁶ If the radicals OR are aliphatic, the intermediate complex breaks down spontaneously, and it is necessary only to distil the mixture to obtain the final product. On the other hand, esters of phenols usually form

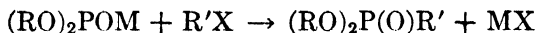
rather stable intermediates, which can be broken down either by drastic heating, such as direct flame heating of the reaction flask,⁵ or by treatment with aqueous alkali, which leads to the same final products in a reaction typical of quasi-phosphonium compounds (see Chapter 11).

Among the more unusual types of this reaction are the following examples. Tri-2-haloethyl phosphites undergo the reaction spontaneously on heating, since they contain both reactive groups in the same molecule. The reaction goes in part by monomolecular route to form the di-2-haloethyl 2-haloethanephosphonates, and partly by polymeric route to form undistillable polyphosphonate esters, which apparently do not contain any alkylenediphosphonate structures.^{113, 114, 115} Diaryl 2-haloethyl phosphites undergo only the bimolecular reaction and form tetra-aryl diphosphonates, $(\text{ArO})_2\text{P}(\text{O})\text{CH}_2\text{CH}_2\text{P}(\text{O})(\text{OAr})_2$, with elimination of ethylene halide. If the diaryl structure is replaced by the *o*-phenylene group, the by-product is vinyl chloride and hydrogen chloride.¹¹⁷ If two alkyl radicals of a tertiary phosphite are replaced by a cyclic ester grouping (a glycol ester), the reaction results in ring opening to yield alkyl 2-haloalkyl phosphonates, provided that the cyclic ester is based on unsubstituted glycol. Substituted glycols usually stabilize the ring structure, and the residual ester group R is lost as RX .⁸⁶ If the glycol radical is replaced by an *o*-phenylene group, the ring ester structure is similarly preserved.⁸⁴ Organo-tin halides react normally to form the organo-tin analogs of phosphonates.^{86, 87} The analogous reaction with secondary haloarsines yields the expected arsinophosphonates.¹²⁶

The principal deviations from the normal course take place in the reactions of the thio derivatives. Tertiary trithiophosphites do not enter the reaction in the usual sense (see Chapter 8). Di-(S)-alkyl benzenedithiophosphonites, $\text{PhP}(\text{SR})_2$, react normally to a large extent, although some monothio derivatives, $\text{PhRP}(\text{O})(\text{SR})$, are usually found among the products; their formation is probably caused by partial air oxidation of the thionothiophosphonates, $\text{RPhP}(\text{S})(\text{SR})$.²² The secondary thiophosphinites, Ar_2PSR , similarly yield by-products of the types $\text{Ar}_2\text{R}_2\text{PX}$ and $\text{Ar}_2\text{P}(\text{O})(\text{SR})$. The $\text{Ar}_2\text{R}_2\text{PX}$ type is formed probably by addition of the reagent halide to the tertiary phosphine, which forms in variable amounts in a side reaction (see Chapters 2 and 5); the $\text{Ar}_2\text{P}(\text{O})(\text{SR})$ type is formed by air oxidation of the initial ester.^{7, 23}

IB. Reaction of organic halides with metal salts of dialkyl phosphites. This reaction, in many ways, is a supplement to the reaction described in Section IA. Although the reaction can be applied, without doubt, to metal derivatives of other analogs of dialkyl phosphites, such as monoesters of phosphonous acids, the scientific literature

contains its application to the phosphite esters exclusively. In its general form the reaction may be shown as:



(Michaelis, Becker; Nylen)

Ordinarily the sodium or the potassium salts of the esters are used. The diethyl or the dibutyl esters have been employed most often; the latter are advantageous because their alkali salts are freely soluble in organic solvents, even of hydrocarbon types.¹³⁷ The general limitations of the nature of the organic halide $\text{R}'\text{X}$ are similar to those given in Section IA, with the following additions. Acyl halides yield substances that have not been identified, whereas dihalides containing secondary halide structures yield olefins.²²² Esters of 2-haloaliphatic acids usually react poorly and tend to yield the Würtz-type products, in a reaction that liberates the dialkyl phosphite radical $(\text{RO})_2\text{PO}$.⁶⁰ If the reaction is conducted with esters of haloacetic acid, however, the resulting trialkyl phosphonoacetates are obtained in good yields. It has been reported that the reaction in this case is best run in absolute ethanol instead of in ether or a hydrocarbon solvent.^{21, 23} The reaction with 1-methoxy-5-chloro-3-pentene proceeds normally, but the isomeric 1-methoxy-3-chloro-4-pentene yields different products, depending on conditions. If free dialkyl phosphite is present, an allylic shift occurs and the phosphono group is attached to the 5-carbon; in the absence of free dialkyl phosphite, the products are polymeric substances of incompletely ascertained constitution.²³² Triarylmethyl chlorides react normally, but the bromides yield free triarylmethyl radicals and $(\text{RO})_2\text{PO}$ radicals when sodium salts of the phosphites are used.¹³ The silver salts yield the normal phosphonates, except for the di-isopropyl derivative, which forms a tertiary phosphite.¹⁰

The metal halide by-product (usually sodium halide) should be removed from the reaction mixture prior to the distillation of the products. Failure to do so results in a secondary reaction, which takes place at about 150 to 200°, in which the ester group is partially replaced by a salt-ester group, $\text{RP}(\text{O})(\text{ONa})(\text{OR})$, with elimination of RX . It is not known whether or not this reaction is a simple displacement. The Arbuzov school prefers to represent this reaction by the addition-cleavage mechanism, similar to that of the usual Michaelis-Arbuzov reaction.²²² The removal of the metal halide, after the customary heating of the reaction mixture for several hours at the boiling point of the solvent, may be accomplished by filtration, centrifuging, or washing with water. The last is preferred for speed of operation, since

the colloidal salts are filtered only with difficulty, although the addition of traces of water facilitates the process.^{21, 137}

IC. Reaction of selected hydroxy derivatives with phosphorus trichloride. Triarylcabinols react anomalously with phosphorus trichloride, as was indicated in Chapter 4. In addition to the formation of the triarylmethanephosphonyl dichlorides described earlier, the reaction mixtures, on treatment with aqueous media, yield small amounts of triarylmethanephosphonic acids. These are believed to be formed from the as yet incompletely understood interaction of the primary adduct of the carbinol and phosphorus trichloride with another molecule of the carbinol. The phosphonic acids, in this instance, do not arise from hydrolysis of the phosphonyl dichloride, which is essentially stable under the conditions used. In contrast to the yields generally obtained from the methods of Sections IA and IB, the yields in the present instance are below 10%; the yield is roughly parallel to the "basicity" of the carbinols used. The reaction is carried out by allowing a mixture of the reactants to stand for a day or two (without heating) and extracting the phosphonic acid by dilute aqueous alkali; acidification yields the desired product.^{11, 29, 54, 55, 99} (Boyd, *et al.*; Hatt; Arbuzov.)

A similar reaction of N-methylol-amides with phosphorus trichloride yields the expected primary dichlorophosphites, ROPCl_2 , which on prolonged standing isomerize into the corresponding phosphonyl dichlorides, RP(O)Cl_2 (see Chapter 4). Usually these are not isolated as such, but the crude reaction mixture is treated with aqueous media, most often very dilute acid or alkali, to yield the phosphonic acid RP(O)(OH)_2 , where R is the acylamidomethyl radical.^{59, 85, 225, 237} (Pikl.)

ID. Reaction of triaryl phosphites with alcohols. When a triaryl phosphite is heated with an alcohol to about 200°, a reaction takes place in which dialkyl alkanephosphonate forms, as shown:

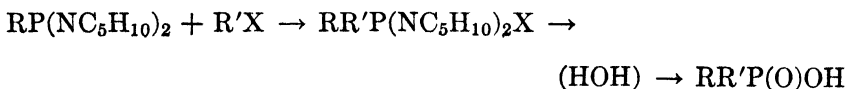


The reaction is carried out preferably with a substantial excess of the alcohol, and yields satisfactory amounts of the phosphonate when a rather small radical R is used.²¹² There is no information on the behavior of the higher alcohols, and, as a matter of fact, the data appear to be in some conflict with patent claims in which ordinary radical exchange is said to take place in reactions of this type (see Chapter 8). (Milobendzki.)

IE. Thermal decomposition of metal salts of dialkyl phosphites. Although thermal decomposition of dialkyl phosphites and of their metal salts, in general, may be expected to yield the most stable aggregate of the component groups, that is, derivatives of phosphonic

acids, the literature contains only one authentic account of such a reaction. When silver diethyl phosphite is heated to above 200° under reduced pressure, some diethyl ethanephosphonate, accompanied by triethyl phosphite, is formed.¹⁰⁹

IF. Reaction of alkyl halides with amides of phosphonous acids. Since amides of phosphonous acids are based on trivalent phosphorus and may be expected to behave in a manner common to such derivatives, it is not surprising that alkyl halides, such as methyl iodide, readily add to these amides to form quasi-phosphonium compounds of N-type. Treatment of these with alkali or with moist silver oxide results in the normal decomposition to the amides of phosphonic acids of secondary type. If the hydrolytic treatment is performed at elevated temperatures, the amide linkage is also cleaved in one operation and secondary phosphonic acid is formed. The reaction should be capable of wide application and gives fair yields.^{184, 231}

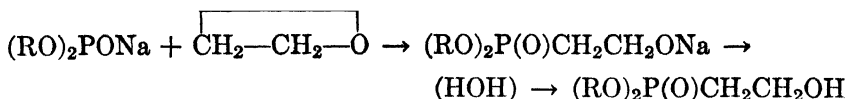


Alkyl diamidophosphites similarly yield primary phosphonic acids.¹⁸⁶

IG. Reaction of selected carbinols with hypophosphorous acid. Treatment of selected carbinols (triarylmethyl carbinols or Michler's hydrol) with hypophosphorous acid results in the formation of the corresponding phosphonous acids and not the esters of hypophosphorous acid as might have been expected. In this respect the reaction bears similarity to the reactions described in Section IC. It is possible that the primary adduct of the carbinol undergoes an isomerization to a structure with carbon to phosphorus bond to yield the most stable configuration under the circumstances, $\text{RP}(\text{O})(\text{OH})\text{H}$.

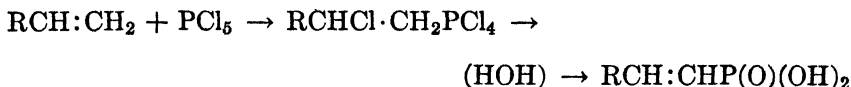
The reaction is best conducted by warming the carbinol with sodium hypophosphite in acetic acid in the presence of sulfuric acid to 50 to 60°, after which the desired acid is removed by extraction with dilute alkali followed by acidification of the alkaline extract. The yields are usually only moderate.^{89, 99} (Fosse; Hatt.)

IH. Reaction of olefin oxides with dialkyl phosphites. Although olefin oxides, like ethylene oxide, are not capable of reacting with the free dialkyl phosphites (see the reaction with phosphine, Chapter 2), a brisk reaction takes place when the sodium salt of the esters is used. Treatment of the reaction mixture, usually in an inert solvent, with dilute acid results in the isolation of dialkyl hydroxyalkanephosphonate, which may be looked upon as the product of ring opening of the oxide, followed by addition.⁶¹ (Chelintsev.)



II. Addition of phosphorus pentachloride to unsaturated linkages

It was pointed out in Chapter 4 that phosphorus pentachloride adds to olefins and to acetylenes in the sense of Cl-PCl_4 , with phosphorus adding to the terminal carbon. Hydrolysis of the resulting products by ordinary treatment with water, followed by partial evaporation of the usual reaction solvent in which the addition was carried out (generally benzene is used), results in the isolation of phosphonic acids. In the strict sense of the word, the reaction considered here is the hydrolysis of the substituted phosphorus tetrachloride. However, since the reaction is usually carried out in a continuous operation, it seems proper to mention it at this point. The general scope of the reaction was indicated in Chapter 4. The principal requirement is that a primary olefin must be used, or at least a compound with a sterically exposed double bond (like indene). The aqueous treatment usually not only converts the tetrachloride into the phosphonic acid but also removes a molecule of hydrogen chloride across the original location of unsaturation, thus giving the final product the structure of unsaturated phosphonic acid. The adducts to acetylene derivatives, however, usually are quite stable in this respect, and hydrolytic treatment merely converts them to 2-halo olefinic phosphonic acids. These may be converted to the acetylenic derivatives by the conventional alcoholic alkali treatment. (Thiele; Bergmann, Bondi.)



Although it has been suggested that the unsaturated compound must be unsymmetric for successful reaction,^{44, 246} it has been shown that symmetric compounds, such as butadiene, are capable of undergoing this reaction sequence.^{45, 138} However, olefins with heavy substitution on the ortho carbons of the phenyl groups attached to the olefinic carbon, as a rule, do not react; the corresponding acetylene derivatives, however, do not display this steric hindrance effect.⁴⁴⁻⁷ The customary use of the phosphorus pentachloride, *per se*, may be replaced by *in situ* preparation, by the passage of chlorine into a solution of the unsaturated compound in phosphorus trichloride.¹⁴⁸ Finally, the hydrolytic step may be replaced by alcoholysis, which yields the corresponding esters of the

phosphonic acids, instead of the free acids.¹³⁸ On the whole, yields of over 50% may be expected in the majority of cases.

III. Reaction of aromatic compounds with phosphorus trichloride in the presence of aluminum chloride

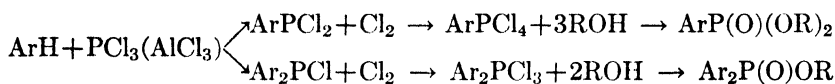
The main basis for this reaction has been discussed in Chapter 3 in the course of the description of a modified Friedel-Crafts method for the synthesis of halophosphines. The usual sequence of oxidative-hydrolytic reactions applied to these derivatives leads to a wide variety of aromatic phosphonic acids. It must be mentioned again that the early low-yield preparations, according to the Michaelis procedure,^{79, 121-2, 152-3, 176, 181, 184-5, 204, 208, 238} cannot be used as absolute criteria for the orientation of the phosphorus atom in respect to the other groups.

A simplified procedure that leads in a continuous operation to the esters of both primary and secondary phosphonic acids has been devised. Very good yields of these products are obtained when the reaction mixture of the aromatic compound with phosphorus trichloride and aluminum chloride, after the requisite period of reflux, is treated with chlorine to break the troublesome halophosphine-aluminum chloride complex, and the resulting mixture is treated with an alcohol under reduced pressure at low temperature. In effect, the reaction procedure forms the dihalogen adducts of the halophosphines, which, in turn, are esterified by the alcohol. The aluminum chloride catalyst is removed after the esterification by water washing. The entire reaction sequence, after the reflux period, is run in a suitable solvent: carbon tetrachloride or, better, tetrachloroethane.

The proportions of the reactants can be varied considerably. Since the fixation of phosphorus occurs at the first step, it is obvious that the general conditions for the synthesis of halophosphines by the Friedel-Crafts reaction may be copied from the available data on this modified procedure. Usually best results for the primary phosphonates are obtained with a substantial excess of phosphorus trichloride (about 3 moles) and with 0.3 to 1.0 mole of aluminum chloride; the reflux period is usually 1 or 2 hours to about 8 hours for the less reactive substances. Lower catalyst proportion lowers the yield drastically, indicating that a three-to-one complex probably forms between the catalyst and the dichlorophosphine. Increase of the reflux period to over 24 hours results in progressively increasing amounts of the secondary phosphonates, indicating catalytic disproportionation of the dichlorophosphines. Similarly, formation of the secondary derivatives is promoted by higher proportion of the aromatic compound in respect to the catalyst. The chlorination of the mixture is performed in the cold, as is the esterifi-

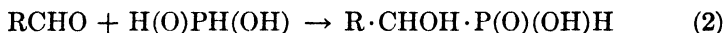
cation step. The elimination of the ligroin extraction procedure, introduced by Michaelis, and the general smoothness of procedure recommend this reaction for the preparation of aromatic phosphonates. Yields of over 80% of the primary phosphonates and of 30% or better of the secondary phosphonates have been reported, when fairly reactive aromatic compounds were used. Dichlorobenzenes are conducive to lower yields; trichlorobenzene appears to be unreactive.¹⁴⁹ It may be mentioned that bromobenzene undergoes partial debromination and the final reaction mixture contains some dialkyl benzenephosphonate, besides the expected *p*-bromobenzene derivative.¹⁴⁶ This finding is in agreement with the work of Mann on reactions of triarylphosphines in the presence of aluminum chloride (see Chapters 2 and 5). (Kosolapoff.)

The over-all representation of the reaction may be shown by



IV. Addition reactions of carbonyl compounds

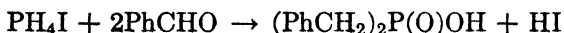
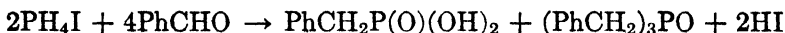
IVA. Addition of carbonyl compounds to substances with a phosphorus-hydrogen linkage. Aldehydes and ketones add to the derivatives of phosphorus in which a real or potential phosphorus-hydrogen bond is present to yield the corresponding hydroxy substituted derivatives. The reaction in its most usual form involves such addition to hypophosphorous acid, phosphorous acid, and phosphonous acids. The typical reactions of an aldehyde are shown below; the ketones react similarly.



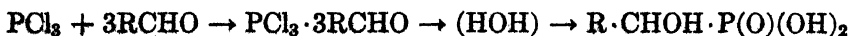
The reaction is conducted by heating the reactants on a water bath for a prolonged period of time, frequently several days. Reactions with phosphorous acid (equation 1) yield hydroxy phosphonic acids that are rather stable to oxidation, and usually no special precautions are needed. Similarly, the formation of secondary phosphonic acids (equation 3) is readily carried out. Reactions with hypophosphorous acid (equation 2), however, are complicated by oxidizability of the primary products. Hydroxy phosphonous acids, and as a rule moderate amounts of the corresponding phosphonic acids, are formed either by atmospheric oxidation or by oxidation-reduction mechanism. In addition, the primary products also are capable of reacting with more of the carbonyl

reagent according to equation 3, thus yielding secondary dihydroxy phosphonic acids. These are usually less soluble than the other components and are readily separated from them. The separation of the hydroxyphosphonous acids from their oxidation products is usually carried out through the lead salts; the salts of the phosphonous acids are much more soluble, and their aqueous solution readily yields the free acids after removal of lead by means of hydrogen sulfide.^{163-174, 253, 254, 256, 257} The yields of the secondary phosphonic acids prepared according to equation 3 are usually good. The reactions with phosphorous acid (equation 1) are not so satisfactory, and the yields are moderate at best. No specific information is available about the yields of the individual compounds obtainable by reactions in accordance with equation 2, because variations in access of air and in the proportions of the reagents seriously affect the amounts of the by-products, which were mentioned above. (Ville; Marie.)

In a rather unusual variation of this reaction, which involved heating benzaldehyde with phosphonium iodide in a sealed tube to 100°, the entire spectrum of primary and secondary phosphonic acids and the tertiary phosphine oxide, in which the expected hydroxyls were reduced to hydrogen atoms, was obtained.¹⁵⁵ The reaction was referred to in Chapter 6. It is probable that the hydroxy derivatives that formed initially were reduced by the hydrogen iodide evolved in the course of the reaction and that the equations that were used to "explain" the total reaction do not give the true picture of the conditions (see below). The acidic components are separated from the phosphine oxide by extraction with aqueous alkali, and the primary phosphonic acid is separated from the secondary acid by its higher solubility in water.

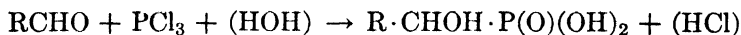


IVB. Addition of carbonyl compounds to halides of trivalent phosphorus. Several experimental variations of this reaction are available. Phosphorus trichloride, combined with 3 moles of an aldehyde in a reaction involving the addition of the reagents and gentle warming, yields upon subsequent treatment with water 2 moles of the aldehyde and 1 mole of a hydroxyphosphonic acid.^{90, 228} The nature of the intermediate adduct has not been established, but it is certain that it is a definite individual substance. After removal of the aldehyde, the desired product is isolated after evaporation of the aqueous solution. (Fossek.)



If an aldehyde or a ketone is added to an equimolar amount (in the actual practice a slight excess is preferable) of a trivalent phosphorus halide, such as PCl_3 , PBr_3 , RPOCl_2 , ROPCl_2 , $(\text{RO})_2\text{PCl}$, and the resulting mixture is in effect hydrolyzed by addition of a substance that has a hydroxy group, such as acetic acid or water (provided that this is added very slowly), the resulting product is a hydroxy substituted phosphonic acid. A similar reaction with secondary halophosphines was given in Chapter 6. Obviously, the use of the chlorophosphites yields not the free acids but the corresponding esters.

The true mechanism of the reaction is unknown, although Conant made several efforts to elucidate it.⁶⁶⁻⁷⁶ Although the final result may be represented by addition through the unshared electrons of the phosphorus atom across the carbonyl group, kinetic studies showed that the rate of formation of such a cyclic adduct is incompatible with the observed facts.⁷⁵ The reaction with phosphorus trichloride is best shown, in the over-all picture, as follows:

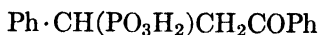
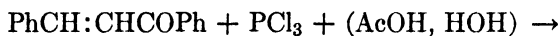


If acetic acid is used for "hydrolysis," the by-product is acetyl chloride and the immediate product is the phosphonyl halide, which on treatment with water yields the hydroxy substituted phosphonic acid. Usually the reaction is performed substantially at room temperature, although the less reactive ketones, such as benzophenone, require the use of benzoic acid and higher temperatures (acetic acid cannot be used at elevated temperatures because it reacts per se with the phosphorus halides).⁷⁸ If acetic acid is used, the binary mixture is treated with a considerable excess of the acid after 2 or 3 hours' standing. If water is used for the hydrolytic step, it is added very gradually to a fresh binary mixture. Addition of water to a binary mixture allowed to stand for a prolonged period of time yields an anhydro acid, most likely a half ester, which was given the denomination of "phostonic" acid by Conant; drastic hydrolysis of the anhydro acid yields the usual hydroxy derivative. The nature of the anhydro acid is as much a puzzle as the over-all reaction mechanism. It is possible that it is a form of a half ester of a polyphosphonic acid, similar to the metaphosphates in the inorganic series. Any mechanism explanation must take into account the actuality of the reaction with three molecules of the carbonyl compound, mentioned above.

Although the reaction proceeds satisfactorily with saturated aldehydes, the saturated ketones usually yield a mixture of the hydroxy acid with the unsaturated acid; separations are usually very difficult.

If water or acetic acid used in the reaction as described above is replaced by acetic anhydride, the immediate product is a phosphoryl halide of the anhydro acid.

The rather similar reaction with unsaturated ketones, in which unsaturation is conjugated with the carbonyl group, provides an additional useful method of synthesis. In this case, treatment of the binary mixture, of the ketone with the phosphorus halide, with acetic acid, followed, after several hours' standing, by aqueous treatment, results in the isolation of keto phosphonic acids, with the phosphono group taking the position on the remote carbon of the double bond, and in effect performing a 1,4-addition across the conjugated system.⁶⁵



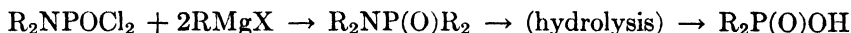
The 1,4-addition is shown clearly by the isolation of an intermediate cyclic anhydrophosphonyl chloride. This can be done only if the "hydrolytically" acting acetic acid is replaced by acetic anhydride. In this case, careful evaporation of the reaction mixture yields this cyclic derivative, usually admixed with a halogen-free material believed to be a dimeric anhydro derivative. The halogen content of the mixture is decreased by higher proportions of acetic anhydride. The precise structure of the presumed dimer has not been definitely proved. However, the intermediate product may be used for the preparation of esters of the corresponding keto phosphonic acids by reactions with alcohols or phenols. Obviously, the use of halophosphines instead of phosphorus trichloride yields the expected secondary phosphonic acids. The general procedure is similar to that used for the saturated carbonyl compounds.^{65, 66, 69, 82, 244} (Conant *et al.*)

Although many compounds have been prepared by the methods shown above, the precise reaction mechanism is not completely clear. It is of interest to note that the intermediate reaction mixtures of all the variations of these procedures are highly viscous and suggest the formation of polymeric intermediates, rather than the monomers indicated.

V. Reaction of Grignard reagents with halides and esters of phosphorus acids

The reaction of Grignard reagents with phosphorus oxychloride goes stepwise, and aqueous treatment of the reaction mixtures yields phosphonic acids and tertiary phosphine oxides. As a rule, the reaction is so rapid that the oxides are formed predominantly, unless the oxychloride

is added to a deficient amount of the Grignard reagent. Even under such conditions the phosphonic acids are formed to but a minor extent. The best procedure involves the reversed order of addition, in dilute solution, followed by aqueous treatment. Reactions of this type yield fairly satisfactory amounts of secondary phosphonic acids and small amounts (or substantially none) of the primary derivatives.^{134, 240} Phosphorus thionohalides, such as PSCl_3 , however, appear to react in a more selective manner, at least with the lower alkylmagnesium halides, and the secondary thiophosphonic acids may be obtained in good yields by ordinary addition and careful hydrolytic treatment.²⁴⁵ Esterification by one molecule of phenol, that is, the use of phenyl dichlorophosphate, is not effective, and the reaction proceeds with displacement of the phenoxy group as well as that of the halogens.²¹⁰ However, blocking of one halogen of phosphorus oxychloride by a secondary amine, such as piperidine or diethylamine, is quite successful, and yields of 70%, or better, of secondary phosphonic acids are readily obtained, after hydrolysis of the intermediate amides by hot hydrochloric acid.^{147, 210} (Sauvage.)



A similar blocking is achieved in effect when phenylated phosphonitrilic dichloride is hydrolyzed by water at 150 to 160°, yielding diphenylphosphonic acid. The phenylation of the phosphonitrilic chloride, PNCl_2 , is performed on the trimer or the tetramer of this curious substance and usually employs the Grignard reagent, although Friedel-Crafts reaction may be used. The phenylation step is most unsatisfactory, in that the yields are poor and the products are non-homogeneous.⁶¹ (Bode.)

Relatively little experimenting has been made on the use of phosphate esters. It has been shown that phenylmagnesium bromide, on prolonged heating with triethyl phosphate to 90° in toluene-ether, slowly yields small amounts of ethyl esters of the corresponding phosphonic acids, which may be hydrolyzed to the free acids: benzenephosphonic acid and diphenylphosphonic acid. In effect, the reaction is a displacement of one or two ethoxyls by phenyl radicals.⁶⁴ (Gilman, Robinson.)

A rather curious method of blocking one chlorine of phosphorus oxychloride has been reported. The phosphorus oxychloride forms an equimolar complex with N-methylacridone, in which one chlorine is essentially inactivated. Treatment of the complex with phenylmagnesium bromide, followed by aqueous treatment, gives excellent yields of diphenylphosphonic acid.⁶⁶

VI. Oxidative phosphonation

The preparation of phosphonyl dichlorides by aeration of hydrocarbon mixtures with phosphorus trichloride was described earlier (see Chapter 4). Hydrolytic treatment of the products yields the corresponding phosphonic acids.⁶² The following reactions, although apparently distinct from the above, are probably intimately connected in terms of the actual mechanism of attachment of the phosphorus atom to the carbon atom. All these reactions start with an oxidizable form of phosphorus. (Willstätter.)

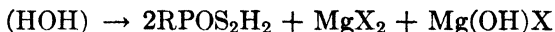
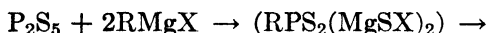
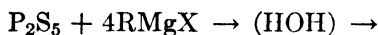
Shaking of an intimate mixture of white phosphorus and an olefin in the atmosphere of oxygen results in a vigorous addition of the components to form intermediates that contain two phosphorus atoms per molecule of the olefin and either three or four oxygen atoms (depending upon the amount of oxygen admitted). The precise structure of the adducts has not been clarified. However, the oxygen addition proceeds in definite steps, and the triatomic adduct is a definite primary product. Careful hydrolysis with water yields a product in which one phosphorus atom is directly bound to a carbon atom of the original double bond, whereas the other phosphorus atom is fairly labile and is apparently bound to the other carbon by an ester linkage. The first phosphorus atom reveals itself at this stage in the form of the phosphonous acid group, the second one in the form of a primary phosphate ester (for the four oxygen atom adduct). Boiling with water cleaves the ester structure, and the product obtained is a hydroxy phosphonous acid, which can be oxidized by nitric acid to the corresponding hydroxy phosphonic acid. The result of the total operation may be crudely described as addition of phosphoric acid, in the sense $\text{HO-PO}_3\text{H}_2$, across the double bond. Although a considerable variety of olefinic substances were successfully treated in the above manner, there is no information about the precise orientation of the groups in the final products. The acids were isolated in the form of lead salts, and no characterizations are possible on this score.^{214, 262}

It is probable that reactions of this general type take place when paraffins are heated with phosphorus to 300 to 350° in inert atmosphere and the resulting products are blown with air at about 100°. ²²⁶ No individual substances have been reported from this procedure. Rather similarly, phosphorus pentasulfide has been reported capable of reaction with olefins at 150 to 180°. The reaction products are acidic and contain sulfur and phosphorus. It is likely that the olefin addition takes place across the phosphorus-sulfur bonds of the pentasulfide to yield mixtures of thio esters and thiophosphonic acids; again no individual substances have been reported.¹²⁹

VII. Grignard reactions with phosphorus sulfides

Some aspects of these reactions were described earlier in connection with the syntheses of phosphines, their sulfides and oxides (see Chapters 2 and 6). It was pointed out at that time that the over-all equations used to illustrate the reaction are pointless, because of the variety of products actually obtained, and that a better visualization of the reaction is given by a "nibbling" attack of the Grignard reagent on the peripheral phosphorus-sulfur bonds of the various sulfides. The yields of individual acids are moderate, at best.

With aliphatic Grignard reagents the reaction with phosphorus pentasulfide yields up to 50% of primary dithiophosphonic acids and up to 20% of secondary dithiophosphonic acids, both after careful hydrolytic treatment of the reaction mixture after refluxing in ether solution. Aromatic Grignard reagents require higher temperatures for the preparation of the secondary acids, usually about 100°. ¹⁶¹ (Malatesta.)

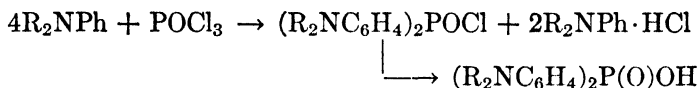


The two principal acid types are separated through the nickel salts. The secondary dithiophosphonates can be extracted readily from water by ether or benzene; the salts of the primary dithiophosphonates are extracted by ether only after acidification. ^{157, 161} When P_4S_3 is used in the reaction, fair amounts of secondary dithiophosphonic acids are formed, especially when an excess of the Grignard reagent is used. The accompanying products include some primary trithiophosphonic acids, $\text{RP}(\text{S})(\text{SH})_2$, although their isolation in the pure state without partial oxygenation is very difficult if not impossible. ¹⁵⁹ The use of P_3S_6 or P_4S_7 gives results of intermediate nature, but with higher yields of accompanying phosphines. The use of ordinary ether reflux temperatures or of higher temperatures (100°) appears to yield different stereoisomers of the secondary dithiophosphonic acids; the exact nature of such isomerism has not been clarified. ¹⁵⁸

VIII. Reaction of dialkylanilines with phosphorus halides

The use of this reaction for the synthesis of phosphine oxides and halophosphines was discussed earlier (see Chapters 3 and 6). When 2 moles of a dialkylaniline are heated to 130 to 160° with 1 mole of phosphorus oxychloride a rather satisfactory amount of the *p*-substituted

primary phosphonyl dichloride is formed, along with varying amounts of di- and trisubstitution. The use of 4 moles of the amine results in higher proportion of the secondary phosphonyl chloride.⁵² Pyridine may be used to replace the amine excess used to bind hydrogen chloride. Careful hydrolysis of the reaction mixture with aqueous alkali, preferably sodium carbonate, yields the corresponding primary and secondary phosphonic acids.⁵² A typical example is shown below. (Bourneuf.)

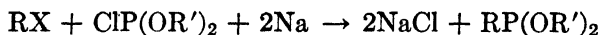


If phosphorus trichloride is used in the above reactions, the resulting intermediate primary and secondary chlorophosphines are hydrolyzed by carbonates to the corresponding phosphonous and phosphinous acids. The former, $RP(O)H(OH)$, are readily separated by their solubility in alkali, whereas the latter, R_2POH , are substantially inert and are salted out by alkali. The last products have been isolated only by careful hydrolysis and are among the rare examples of phosphinous acids.^{52, 208, 234} (Michaelis, Schenk.)

Usually the excess base is removed by steam distillation, prior to the isolation of acidic components.

IX. Würtz reaction with phosphorus halides

Very few examples of such reactions have been reported. A claim was made in the patent literature that the usual Würtz reaction with metallic sodium, on the one hand, and with a mixture of halogenated organic compound and secondary chlorophosphite, or primary dichlorophosphate, on the other hand, yielded the corresponding esters of phosphonous or phosphonic acids.⁸⁴ For example,



A somewhat different approach was made in the reaction of sodium with a mixture of bromobenzene and a dialkylamidodichlorophosphate. The resulting amide of the secondary phosphonic acid can be hydrolyzed readily with hot hydrochloric acid to the corresponding free acid.¹⁸⁶ (Michaelis.)



X. Oxidation of phosphines

Air oxidation of primary phosphines results in a pick-up of two atoms of oxygen with the resultant formation of phosphonous acids, RPO_2H_2 .¹⁰² More vigorous oxidation, which undoubtedly proceeds through this stage, gives phosphonic acids (see Section XI). Secondary phosphines oxidize rapidly to the secondary phosphonic acids, even on exposure to the air, and the isolation of the possible intermediates, phosphinous acids, is impossible. (Hofmann.)

XI. Oxidation of phosphonous acids, phosphinous acids, and their esters

As was mentioned above, oxidation of primary phosphines by the more effective oxidizing agents, such as nitric acid, potassium permanganate, or alkali dichromates, probably proceeds through the stage of formation of the corresponding phosphonous acids. These are readily attacked further and yield the primary phosphonic acids, $\text{RP}(\text{O})(\text{OH})_2$.

In the specific oxidation of phosphonous acids to phosphonic acids, which may be resorted to in some cases, the same oxidizing agents may be used when the radical of the acid is unsubstituted. A more convenient oxidation is achieved with sulfur dioxide, which is used in gaseous state, or with a solution of mercuric chloride, which is reduced to calomel in the process.^{133, 179, 188} The latter procedure is of particular value in the oxidation of hydroxy phosphonous acids and the dialkylamino-benzene derivatives.^{52, 166, 234} The oxidation of hydroxy substituted phosphonous acids to the corresponding phosphonic acids is achieved in the most satisfactory manner by the addition of bromine water to the solution of the acid in water. The solution must be evaporated to yield the product without added purification.¹⁶⁸

Esters of phosphonous or phosphinous acids are readily oxidized to the corresponding phosphonates by blowing with oxygen; less effective is oxidation by air current.¹⁹⁹ A smoother reaction results from the addition of one mole of bromine, followed by treatment with water or alcohol.¹⁹⁹



XII. Hydrolysis of halophosphines

Primary dihalophosphines react smoothly with water to yield the corresponding phosphonous acids, RPO_2H_2 . If the reaction mixture is not allowed to reach unduly high temperatures, the oxidation reduction of the phosphonous acids may be kept to negligible proportions (see Section XXI). (Michaelis.)

Hydrolysis of secondary monohalophosphines, however, yields the expected phosphinous acids, R_2POH , only on very rare occasions. Specifically in the aromatic series the *p*-dialkylamino derivatives are capable of such reaction.²²⁹ Usually, however, the products undergo the oxidation reduction spontaneously, essentially at room temperature, and yield a mixture of the secondary phosphine, R_2PH , and secondary phosphonic acid, $R_2P(O)OH$. The reaction is facilitated by the use of aqueous alkali.²²⁹ Hydrolysis of the secondary monohalophosphines by dilute nitric acid is a common method for their conversion into the secondary phosphonic acids. In this case the phosphine is simultaneously oxidized, and the over-all result is the formation of but one product.^{180, 199} (Michaelis; Plets.)

A curious form of hydrolysis takes place when phenyldichlorophosphine is treated with one mole of hot water and the mass is heated to 200°. The resulting mixture contains a little benzenephosphonous acid, some benzenephosphonic acid, and much diphenylphosphonic acid. This form of hydrolysis obviously requires a translocation of the phenyl radical, accompanied by oxidative changes. The mechanism of this reaction, which does not appear to be the usual oxidation reduction of phosphonous acids, is unknown.¹⁹³

XIII. Hydrolysis of phosphonyl halides and of halophosphine dihalides

Hydrolysis of primary and secondary phosphonyl halides, $RP(O)X_2$ and $R_2P(O)X$, by means of warm water yields the corresponding phosphonic acids. The use of aqueous alkali yields the corresponding salts. The course of the hydrolysis may not be a simple exchange of halogen atoms for hydroxyls. It is possible that coordination of water to the semipolar oxygen first yields a quasi-phosphonium compound, which then suffers the usual decomposition. The thionophosphonyl halides, $RP(S)X_2$ and $R_2P(S)X$, as a rule yield only moderate amounts of the thiophosphonic acids on aqueous hydrolysis, as prolonged heating with water gradually converts them into the sulfur-free phosphonic acids.¹⁹⁶ This conversion indicates a strong possibility of the quasi-phosphonium hydrolytic mechanism that was indicated above. "Hydrolysis" of secondary thionophosphonyl halides with potassium sulfide in alcohol yields the secondary dithiophosphonic acids, R_2PS_2H .¹⁸⁸ RPX_4 and R_2PX_3 derivatives hydrolyze similarly.

The principal exception to the usually mild hydrolysis of phosphonyl halides is found among triarylmethanephosphonyl dichlorides. These can be hydrolyzed to the phosphonic acids only by drastic methods. Commonly, the halide is warmed with alcoholic potassium hydroxide;

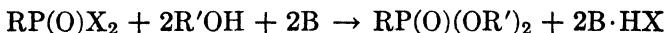
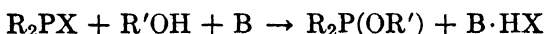
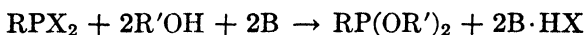
the resulting crude mixture, containing some phosphonic acid and the half ester in the form of alkali salts, is heated with acetic acid-hydriodic acid mixture.

XIV. Hydrolysis of esters of phosphonic acids

The esters of phosphonic acids are readily hydrolyzed by hot hydrochloric or hydrobromic acid. With concentrated acids the ester group is eliminated as an alkyl halide. The concentrated acids may be used for almost all types of phosphonates, with the exception of esters of alkoxymethane acids, which suffer ether link cleavage. In such cases, either dilute acid (in sealed tubes at 130 to 150°) or aqueous alkali may be used. It should be noted that 1-keto phosphonates cannot be hydrolyzed without cleavage of the carbon to phosphorus bond; hence the free acids of acylphosphonic, phosphonoformic, and phosphonomalonic types cannot be obtained. Trichloromethanephosphonates are also in this category.

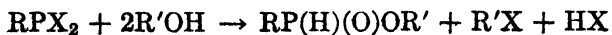
XV. Esterification of halophosphines and phosphoryl halides

The most satisfactory esterification of these compounds in the laboratory is achieved by the addition to the desired alcohol, or phenol, in the presence of the theoretical amount of a tertiary base, usually pyridine or dialkylaniline.^{33, 149} In this manner the neutral esters of phosphinous, phosphonous, and phosphonic acids are formed in good yields.



Somewhat less satisfactory results are obtained with sodium alkoxides since the separation of colloidal sodium halide is cumbersome and side reactions, caused principally by free alkali in the alkoxides, tend to give by-products, such as salts or isomerization products of phosphonites and phosphinites.^{6, 8, 9, 139, 229} The isomerization products are the only substances that can be isolated from such reactions of secondary halophosphines with sodium methoxide; the derivatives of benzyl alcohol and benzyl thiol behave similarly.⁷ (Michaelis; Arbuzov.)

Addition of primary dihalophosphines to dry alcohols in the cold and prolonged evacuation of the mixtures leads to the formation of monoalkyl esters of phosphonous acids, in a manner similar to the formation of dialkyl phosphites from phosphorus trichloride (see Chapter 8).



The direct action of phosphonyl halides on alcohols results in the formation of neutral esters only if the reaction is run with an excess of the alcohol at moderate temperatures and under reduced pressure.^{149, 248} In such cases excellent yields are obtained; the use of elevated temperature leads to substantial amounts of by-products, principally partial esters. Phenols are usually esterified by heating (in contrast to the alcohols), and stepwise esterification may be achieved with phosphonyl dihalides.^{179, 195} Thionophosphonyl dihalides may be converted to half esters, $RP(OR')S_2H(?)$, by heating with potassium hydrosulfide solution in the desired alcohol.¹⁶⁰

The polyhalides, RPX_4 and R_2PX_3 , react smoothly with 3 or 2 moles of an alcohol or phenol, respectively, and form the corresponding phosphonates.^{149, 179, 195} The remaining halogen atom is eliminated in the form of halide, $R'X$, in the ensuing decomposition of intermediate quasi-phosphonium compounds. (Michaelis; Kosolapoff; Toy.)

XVI. Oxidation of compounds with phosphorus to sulfur linkage

Drastic oxidation of any substance that has one or two organic radicals attached to the phosphorus atom, the remaining valence(s) being bound to sulfur in any form, results in the formation of the corresponding primary or secondary phosphonic acids, with elimination of sulfur. The reagents used are usually hot nitric acid^{132, 161} or bromine water¹⁶¹ or sodium hypobromite.¹⁵⁹ Reactions of this type may be used to form phosphonic acids from the products of sulfur addition to phosphines.¹³²

XVII. Reaction of phosphorus pentachloride with selected carbonyl compounds

Treatment of some carbonyl compounds results in the formation of phosphonic acids after aqueous treatment of the reaction mixtures. Thus acetophenone treated with phosphorus pentachloride in the cold, followed by quenching in ice water, yields a small amount of 2-phenyl-2-keto-1-dichloroethanephosphonic acid, $Ph \cdot CO \cdot CCl_2 \cdot P(O)(OH)_2$.⁴³

A similarly minute yield of a phosphonic acid is secured by heating N-acetyldiphenylamine with the pentachloride and treating the mixture with water. The product is 1-chloro-1-diphenylamino-ethanephosphonic acid.⁹²

Information on the structural requirements for such reactions is non-existent.

XVIII. Reaction of some nitrogen heterocycles with phosphorus oxychloride

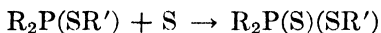
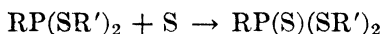
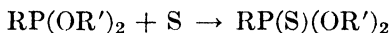
The only example on the record is the direct phosphonation of 1-phenyl-3-methyl-5-chloropyrazole in the 4-position by heating with

phosphorus oxychloride to 130 to 150°, followed by aqueous treatment.²⁰⁵

XIX. Addition of sulfur to primary and secondary phosphines and to the esters of phosphonous and phosphinous acids

Warming primary phosphines with elemental sulfur results in products that may be regarded as primary thiophosphinous acids, RPSH_2 or $\text{RPH}(\text{SH})$. Only the product from phenylphosphine has been characterized at all satisfactorily. The reaction with secondary phosphines is clearer. The products are secondary dithiophosphonic acids, $\text{R}_2\text{PS}_2\text{H}$, obtained by the addition of two atoms of sulfur. It is probable that the true primary adducts are polysulfides that are cleaved in the course of isolation of the acids (usually treatment with aqueous alkali).^{158, 192} Sulfur is added by heating in inert atmosphere, because of the oxidizability of the phosphines on air exposures.¹⁵⁸ (Michaelis.)

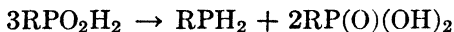
Esters of phosphonous acids and phosphinous acids, as well as the corresponding thio derivatives, add sulfur readily on heating, in the usual manner, as true trivalent phosphorus derivatives.²²



The resulting products are esters of the thiophosphonic acids.

XX. Disproportionation or oxidation reduction of phosphonous acids

Phosphorus compounds of intermediate oxidation states usually undergo thermal disproportionation or oxidation reduction on heating. The most common reaction is that undergone by phosphonous acids on heating; the products are primary phosphines and phosphonic acids.¹⁷⁹



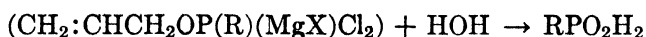
Usually the crude hydrolysis product of the dihalophosphine is used in this reaction. The heating range is from 70 to 80° for aliphatic compounds to 130 to 170° for the aromatic derivatives. Although such a reaction is regarded as an intermolecular, it is most probable that phosphonous acids, as other keto forms of hydroxyphosphines, exist in dimeric or trimeric state of association, bound by hydrogen bonds. Such an aggregate, probably cyclic in structure, needs but a moderate shift of the linkages to effect such oxidation reduction within the ring. As a rule, this is a poor synthetic method, complicated by the evolution of malodorous phosphines.^{182, 196} (Michaelis.)

XXI. Reaction of alkyl halides with silver phosphonates

The classical esterification of silver salts of acids by alkyl iodides has found little practical use among the phosphorus acids. A few old preparations of dialkyl phosphonates by this method are on record. The reaction consists of the usual heating of the reactants, filtration of silver iodide, and distillation of the ester.

XXII. Reaction of Grignard reagents with allyl dichlorophosphite

This reaction was isolated from those in Section V because it appears to be a unique method for the synthesis of phosphonous acids. Allyl dichlorophosphite reacts readily with Grignard reagents, and the resulting mixture yields, on treatment with ammonium chloride solution, phosphonous acids carrying the radical of the Grignard reagent. The products are isolated by extraction with aqueous alkali and acidification.²²⁶ Fairly good yields are reported for a variety of phosphonous acids. Unfortunately, no information is available concerning the limitations of this reaction. (Plets.)

**XXIII. Reaction of sodium hypophosphite with diazonium chlorides or substituted hydrazines**

The only available information about these reactions comes from a single laboratory.^{227, 228} Private reports received by the author indicate the possible failure of the originator of these reactions to include all the necessary conditions, as the syntheses could not be duplicated. In essence, the reported procedures are as follows. Aromatic diazonium chlorides are added to solutions of sodium hypophosphite in the presence of a little copper sulfate. After the evolution of nitrogen is finished, the filtrate from tarry residue yields phosphonous acids that carry the radical of the diazonium salts used. Yields of 20 to 30% have been reported.^{227, 228} The advantages of such reaction are obvious; various substituted phosphonous acids that cannot be obtained otherwise are made available. Monoaryl hydrazines are also reported to give such products in a reaction conducted in identical manner.^{227, 228} (Plets.)

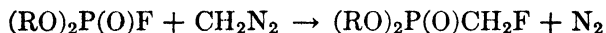
XXIV. Reaction of diphenylamine with phosphorus trichloride

This reaction, first reported several decades ago, has been cleared only recently.²⁴¹ Heating diphenylamine with an equimolar amount of phosphorus trichloride to about 200° and hydrolysis of the mixture with

hot water yield a cyclic product: phenophosphazinous acid (or hydroxy-phenophosphazine). Apparently the primary product of the reaction, diphenylamidodichlorophosphite, undergoes extensive rearrangement and further condensation at the ortho carbons. The yield of this product is poor, and the nature of residual matter is unknown. Air oxidation of the product readily yields the corresponding phosphonic acid of cyclic structure.²⁴¹ (Michaelis; Sergeev *et al.*)

XXV. Reaction of diazomethane with halophosphates

Dialkyl fluorophosphates react smoothly with diazomethane and form the corresponding dialkyl fluoromethanephosphonates.²³⁹ (Saunders.)



GENERAL CHARACTERISTICS

The majority of the reactions that occur in the class of compounds discussed in this chapter are contained in the previous section; thus this chapter is self-contained so far as possible. The following remarks cover items not mentioned in the synthetic procedures.

Primary and secondary phosphonic acids are, as a rule, crystalline substances that have, respectively, dibasic and monobasic functions. They are among the most stable derivatives of phosphorus in terms of thermal treatment. On strong heating some anhydride formation takes place, but only heating to very high temperatures results in cleavage of the carbon-phosphorus linkage. The principal exceptions to the stability rule are the 1-keto acids, which undergo spontaneous decomposition upon hydrolysis of their esters, and the phosphonomalonic and phosphonoformic acids, which suffer the same fate. Since these acids and their esters are based on phosphorus in the highest oxidation state, many of the usual organic transformations can be performed with these compounds to form additional derivatives not obtainable by direct methods. Among the aliphatic compounds rather little work of this type has been done by the usual replacement reactions. A reaction that deserves special notice is the formation of potassium or sodium derivatives by the esters of phosphonoacetic acid, very similar to the reaction of malonic ester. The metal derivatives react with alkyl halides and may be readily converted to the corresponding esters of phosphono-alkylacetic acids, $(\text{RO})_2\text{P}(\text{O})\text{CHR}\cdot\text{CO}_2\text{R}$. The potassium derivatives are usually most satisfactory. The aromatic phosphonic acids undergo the usual aromatic substitutions, with the apparently

exclusive substitution in the meta position of the benzene ring, in respect to the point of attachment of the phosphorus atom. The investigation of these "secondary" derivatives indicates that amino groups in ortho or para positions loosen the carbon to phosphorus linkage so much that it is readily broken by treatment with bromine water, with replacement of the phosphorus by bromine.

Phosphonous acids, RPO_2H_2 , are usually sirups in the aliphatic series but crystalline solids in the aromatic family. They are monobasic acids and thus have the keto structure typical of hydroxy derivatives of trivalent phosphorus. As such they are formulated as RP(O)H(OH) , a structure suggesting possible association by hydrogen bonding into cyclic dimers or trimers, analogous to the dialkyl phosphites. These acids cannot undergo many of the usual organic substitutions as they are subject to oxidative attack by such reagents as the halogens and nitric acid. The dialkyl esters of these acids are based on trivalent phosphorus and possess the usually strongly expressed additive tendencies. Mild hydrolysis of these esters forms the monoesters that no longer possess the true trivalent phosphorus structure but must be formulated as RP(O)(OR)H . The relationship of these substances with the esters of phosphorous acid is strikingly shown by these manifestations. The phosphinous acids and their esters show the same type of keto-enol behavior. As a matter of fact, Arbuzov formulated a general rule that a true hydroxyl cannot exist on a trivalent phosphorus atom and must rearrange, immediately, into the keto form, P(O)H . This rule is rather useful so far as the interaction with aqueous alkaline reagents is concerned. There is little doubt, however, that the singular hydrogen in all these substances is directly replaced by alkali metals under anhydrous conditions and that the term "acidity" is a relative one, for under the proper conditions the "acidic" nature of the singular hydrogen can be manifested.

The thio analogs of the above acids present some problems that have not been solved to this day. Acids that have oxygen atoms as well as sulfur atoms at the central phosphorus atom cannot be assigned a definite location of the proton (or of the cations in the case of salts). It is, however, likely that the proton and cation attachment is largely centered at the sulfur rather than at the oxygen. The organic solvent solubility of the metal salts and the general tendency of oxygen to replace semipolarly bound sulfur in the various isomerization reactions of phosphorus compounds appear to be valid reasons for this assumption. Because of the lability of sulfur under oxidative-hydrolytic conditions essentially nothing has been done on the preparation of substitution derivatives among these substances. Mild oxidation of these acids

results in the formation of disulfides or thioanhydrides. Few of them have been characterized, and these are referred to Chapter 12.

It is important to add the following warning. A number of the substituted aromatic derivatives in this family were prepared from the dihalophosphines, obtained in turn by the Friedel-Crafts reaction from the respective aromatic compounds, using the inefficient extraction procedure (see Chapter 3). It is very likely that the use of the newer methods^{83, 149} may reveal heterogeneity and presence of other isomers in such cases, when the entire reaction mixture is utilized. This warning should apply to much of the older work.^{78, 82, 97, 128, 152, 180-208, 230, 260-261}

The substances described in this chapter offer many interesting possibilities from the practical point of view. Phosphonic acids and their esters, being substances of a high order of stability with few individual exceptions, resemble in their general properties the corresponding esters of phosphoric acid, many of which have found practical applications. The salts of phosphonic acids and of their thio analogs possess manifestations of surface activity, best expressed in derivatives with large organic radicals. Heavy metal salts of the secondary phosphinic acids have appreciable solubility in organic solvents, making them attractive for applications in non-aqueous systems. The neutral esters of phosphonic acids open a wide field of new plasticizers, which appear to be more stable at high temperatures than the corresponding tertiary esters of phosphoric acid. The plasticizer and solvent action depends largely upon the hydrogen bonding ability of the oxygen of the PO group in both classes of these compounds. At the present time, however, the determination of the quantitative aspect of this ability has been measured only for the phosphates and only to a limited extent. No quantitative data may be found on the hydrogen bonding tendency among the phosphonates at this time.

The acids of the lower stages of oxidation, and particularly their esters that are constituted on the basis of trivalent phosphorus, possess varying degrees of oxidizability and as such have been suggested as antioxidation agents in several patent claims. The aminosubstituted aromatic acids appear to have biological activity; phosphonous acids of this type have been disclosed in patents as useful medicinal agents. It is of interest to note that *p*-aminobenzenephosphonous acid has a much higher sulfanilamide-like activity than the corresponding phosphonic acid. This finding, by Klotz and Morrison, appears to indicate that this substance is more akin to *p*-aminobenzoic acid in its biochemical functions than the acid having two ionizable hydrogen atoms. As such, it indicates a new and interesting line of research in pharmaceutical and biochemical sciences. Investigations along similar lines by Smith

and co-workers at the U. S. Public Health Service disclosed some anti-tubercular action by bis-(dimethylaminophenyl)phosphonic acid, again substantiating the above-mentioned higher biochemical activity of a monobasic acid in comparison with a dibasic acid of analogous constitution. The ever-growing fund of data on the importance of phosphorus derivatives in normal and abnormal metabolism may well be supplemented in the years to come by the information to be gathered from substances assembled in this chapter.

PHOSPHONOUS ACIDS

COMPOUNDS WITH THE PHOSPHORUS ATOM JOINED TO AN ALIPHATIC CARBON

- MePO₂H₂.** X. Oil.¹⁰²
- EtPO₂H₂.** X.¹⁰² XII.⁹⁷ XXII.²²⁶ Oil; d^{19} 1.2952.⁹⁷ Best isolated as the poorly soluble lead salt.²²⁶
- PrPO₂H₂.** XII. Oil; d^{13} 1.1418.⁹⁷
- CH₂:CH·CH₂PO₂H₂.** XXII. Hygroscopic crystals, dec. 120°. ²²⁶
- iso-PrPO₂H₂.** XII. Oil; d^{19} 1.1891.⁹⁷
- iso-BuPO₂H₂.** XII. Oil; d^{23} 1.0740.⁹⁷
- iso-AmPO₂H₂.** XII.⁹⁷ XXII.²²⁶ Oil; d^{23} 1.0613.⁹⁷ Best isolated as the poorly soluble lead salt.²²⁶
- n-C₇H₁₅PO₂H₂.** X. Oil, obtained only in crude state.²⁵⁹
- n-C₈H₁₇PO₂H₂.** X. Oil.²¹⁶
- PhCH₂PO₂H₂.** X. XII. Water-soluble oil.¹⁵¹
- Ph₃CPO₂H₂.** IG. Crystals, m. 94°(?),⁸⁹ m. 245-8° (from EtOH).⁹⁹
Methyl ester. XXI. Crystals, m. 163-4°. ⁹⁹
- (4-Me₂NC₆H₄)₂CHPO₂H₂.** IG. Crystals, m. 110° (from EtOH).⁸⁹
- Me·CHOH·PO₂H₂.** IVA. Oil; dec. 130°. Barium salt: water-soluble crystals, appreciably soluble in alcohol.²⁶⁷
- Me₂COH·PO₂H₂.** IVA.^{163, 165, 173, 174} Hygroscopic crystals, m. 52° (from water).^{165, 174}
Best purified through its water-soluble lead salt.¹⁶³ Decomposes at 110-20°. ¹⁶⁵
The copper salt yields, on heating to 100° in inert atmosphere, free copper and some of the corresponding phosphonic acid.¹⁶⁵
Methyl ester. XXI. Undistillable oil; $d^{16.5}$ 1.212.¹⁶⁵
Ethyl ester. XXI. Undistillable oil; $d^{22.5}$ 1.122.¹⁶⁵
- MeEtCOH·PO₂H₂.** IVA.^{170, 174} Oil; dec. 100°. ¹⁷⁰ Lead salt: crystals (from dil. EtOH).¹⁷⁰
- MePrCOH·PO₂H₂.** IVA.^{171, 174} Oil; dec. about 100°. ¹⁷¹ Lead salt: crystals (from EtOH).¹⁷¹
- Et₂COH·PO₂H₂.** IVA. Oil. Lead salt: crystals soluble in alcohol.¹⁷³
- iso-Bu·CHOH·PO₂H₂.** IVA. Oil; dec. 170°. ^{266, 267} Barium salt: crystals, soluble in water.²⁶⁷
- n-C₆H₁₃·CHOH·PO₂H₂.** IVA.^{100, 266, 267} Plates, m. 55-7° (from Et₂O); dec. 120.^{100, 267}
Acetate: oil.^{266, 267}

Ph·CHOH·PO₂H₂. IVA.^{168, 256, 257} Plates, m. 108°¹⁷⁴ (the older value, m. 90°, is inaccurate). Decomposes at 140°.^{168, 256}

Acetate. An oil prepared by means of acetyl chloride.²⁵⁷

Methyl ester. XXI. Crystals, m. 99°; benzoate: m. 93°.¹⁷⁴

Ph₂COH·PO₂H₂. IVA.^{171, 174} Plates, m. 150–1° (from water).^{171, 174} Lead salt: soluble in organic solvents; insoluble in water.¹⁷¹

MePhCOH·PO₂H₂. IVA.^{172, 174} Crystals, m. 85°¹⁷⁴ (the older value, m. 78°,¹⁷² is inaccurate). Decomposes at 100°. Lead salt: crystals, soluble in alcohol, almost insoluble in water.¹⁷²

(2-HOC₆H₄)·CHOH·PO₂H₂. IVA. Resin, soluble in water and alcohol, but insoluble in ether and chloroform.²⁵⁷

(4-iso-PrC₆H₄)·CHOH·PO₂H₂. IVA. Plates, m. 105°.²⁵⁷

Me·CO·CH₂PO₂H₂. Isolated only as a crude barium salt (soluble in water) from the distillation residues of a mixture of acetone, phosphorus, and iodine.²¹⁸ The identity of the product appears to be questionable.

(1,3-)C₆H₄(CHOH·PO₂H₂)₂. IVA. Isolated as a crystalline, water-soluble disodium salt.¹⁰⁰

COMPOUNDS WITH THE PHOSPHORUS ATOM JOINED TO AN AROMATIC CARBON

PhPO₂H₂. X.^{132, 133} XII.^{133, 179, 188} XXII.²²⁶ XXIII.²²⁷ Plates, m. 70° (from water),¹⁷⁹ m. 70.5°,²²⁷ m. 71°.²²⁶ Phenylhydrazine salt, m. 135°; *p*-tolylhydrazine salt, m. 148°; phenylbenzylhydrazine salt, m. 108°.²⁰¹

Dimethyl ester. XV.^{9, 38, 126} b₁₅ 101–2°,⁹ b₁₃ 94.5°,³⁸ d₀¹⁶ 1.1022,⁹ d₀¹⁶ 1.0972,³⁸ d₀²⁰ 1.0849,⁹ d₀²⁴ 1.0732,³⁸ n_D²⁰ 1.5118(?),¹²⁶ n_D²⁰ 1.5280,⁹ n_D²⁷ 1.5186.³⁸ CuBr salt: crystals, m. 139.5–40°.⁹

Diethyl ester. XV.^{9, 38, 126, 133} b. 235–7°,^{38, 133} b_{10–13} 110–1°,¹²⁶ d₀¹⁶ 1.0405,¹²⁶ d₀¹⁶ 1.032,^{9, 8} d₀²⁰ 1.0247, n_D²⁰ 1.5120,³⁸ n_D⁰ 1.5063(?).¹²⁶

Di-isopropyl ester. XV.²⁴ b₁₀ 121–2°, d₀¹⁶ 1.0103, d₀¹⁷ 0.9952, n_D¹⁸ 1.5021.²⁴

Dipropyl ester. XV.³⁸ b₁₅ 137°,³⁸ b_{10–3} 132.5–3.5°,¹²⁶ d₀¹⁶ 1.0123, d₀²³ 0.9925, n_D²⁶ 1.4939.³⁸

Di-isobutyl ester. XV.^{8, 12, 126} b_{11.5} 148–8.5°,⁸ b_{10–3} 144–5°,¹²⁶ b₇ 134.5°,¹⁸ d₀¹⁶ 1.0060, n_D¹⁶ 1.4658.¹²⁶

4-ClC₆H₄PO₂H₂. XII. Needles or plates, m. 130–1°,¹⁸⁴ m. 131° (from water).³⁹ Phenylhydrazine salt: m. 169°.¹⁸⁴

4-BrC₆H₄PO₂H₂. XII.¹⁸⁴ XXIII.²²⁷ Plates, m. 143° (from EtOH).^{184, 227} Phenylhydrazine salt: m. 181°.¹⁸⁴

4-MeOC₆H₄PO₂H₂. XII. Needles, m. 112°,¹⁸⁴ m. 114–4.5° (from water).¹²² Aniline salt: m. 97–8°; *p*-toluidine salt: m. 99–100°;¹²² phenylhydrazine salt: m. 116°.¹⁸⁴

4-EtOC₆H₄PO₂H₂. XII. Plates, m. 115°.¹⁸⁴

2-O₂NC₆H₄PO₂H₂. XXIII. Needles, m. 157° (from Et₂O-MePh).²²⁷

4-O₂NC₆H₄PO₂H₂. XXIII. Plates, m. 134° (from Et₂O-MePh).²²⁷

4-H₂NC₆H₄PO₂H₂. By heating the corresponding bromo derivative (see above) with ammonium hydroxide in the presence of cuprous oxide. Crystals, m. 169°, sol. 5% in water at 0°; *pK* 3.68.¹²⁰

4-Me₂NC₆H₄PO₂H₂. XII.^{106, 207, 208} Better prepared by VIII.^{53, 234} Needles, m. 162°,^{207, 208} m. 163°,^{53, 234} (from water, after conversion to the lead salt and treatment with hydrogen sulfide). Either the copper or the lead salt may be used in the purification. Sodium salt (dihydrate): plates (from abs. EtOH).^{106, 207} The acid is poorly stable in acid solutions.

- 4-(PhCH₂)MeNC₆H₄PO₂H₂.** XII. Needles, m. 96° (from dil. EtOH). Sodium salt (dihydrate): needles, m. 233° (from EtOH).²⁰⁸
- 4-PhMeNC₆H₄PO₂H₂.** XII. Needles, m. 150–50.5° (from EtOH). Sodium salt (dihydrate): plates, m. 265° (from EtOH).²⁰⁸
- 4-Et₂NC₆H₄PO₂H₂.** XII. Oil.²⁰⁸
- 4-(Me₂N)-2-MeC₆H₃PO₂H₂.** VIII. Sodium salt (trihydrate): plates or needles (from EtOH).¹⁰⁶
- 4-(Et₂N)-2-MeC₆H₃PO₂H₂.** VIII. Sodium salt (trihydrate): prisms (from EtOH).¹⁰⁶
- 3-MeC₆H₄PO₂H₂.** XII. Oil. Phenylhydrazine salt: m. 131°. ¹⁸⁴
- 2-MeC₆H₄PO₂H₂.** XII.²⁰⁴ XXIII.²²⁷ Plates, m. 115°. ²²⁷ (Oil ²⁰⁴).
- 4-MeC₆H₄PO₂H₂.** X.²⁰⁴ XII.²⁰⁴ XXIII.²²⁷ Plates, m. 104–5°, ²⁰⁴ m. 106° ²²⁷ (from EtOH). Phenylhydrazine salt: m. 161°. ²⁰¹
- Diethyl ester. XV. Oil; b. 280°. ²⁰⁴
- 4-Me-3-ClC₆H₃PO₂H₂.** XII. Needles, m. 70° (from benzene).¹⁷⁶ Phenylhydrazine salt: m. 156.5°. ¹⁷⁶
- 4-EtC₆H₄PO₂H₂.** XII. Plates, m. 63–4° (from water).¹⁸⁴ Phenylhydrazine salt, m. 133°. ¹⁸⁴
- 2,4-Me₂C₆H₃PO₂H₂.** XII. Needles, m. 100° (from water).^{184, 204}
- 2,5-Me₂C₆H₃PO₂H₂.** XII. Needles, m. 97–8° (from EtOH).²⁶¹
- 2,4,5-Me₃C₆H₂PO₂H₂.** XII. X (less satisfactory). Plates, m. 128° (from EtOH). Phenylhydrazine salt: m. 180°. ¹⁸⁴
- Diethyl ester. XV. Oil, b₁₀₀ 232–3°, n_D¹⁵ 1.505, d¹⁵ 1.048. ¹⁸⁴
- Diphenyl ester. XV. Crystals, m. 59°, b₄₀ 283°, supercooled: n_D¹⁵ 1.5085, d¹⁵ 1.144. ¹⁸⁴
- 2,4,6-Me₃C₆H₂PO₂H₂.** X. XII. Needles, m. 147° (from water). Phenylhydrazine salt, dec. 132°. ¹⁸⁴
- 4(?) -iso-PrC₆H₄PO₂H₂.** XII. Oil. Neutral phenylhydrazine salt, m. 161°; acid phenylhydrazine salt, m. 135°. ¹⁸⁴
- 2(or 5)-Me-5(or 2)-iso-PrC₆H₃PO₂H₂.** XII. Oil. ¹⁸⁴
- 1-C₁₀H₇PO₂H₂.** XII.¹⁵² XXIII.²²⁷ Needles, m. 125–6°, ¹²⁸ m. 137°, ¹⁶² m. 138° (from water). ²²⁷
- 2-C₁₀H₇PO₂H₂.** XXIII. Plates, m. 175°. ²²⁷
- 4-PhC₆H₄PO₂H₂.** Obtained only as a mixture of isomers. XII. Crystalline powder. ¹⁸⁵
- 4-PhCH₂C₆H₄PO₂H₂.** XII. Crystals, m. 84° (from EtOH).¹⁸⁵ Phenylhydrazine salt, m. 171°. ¹⁸⁵
- 4-PhCH₂CH₂C₆H₄PO₂H₂.** XII. Plates, m. 156–7° (from dil. EtOH).¹⁸⁵
- Dibenzofuran-3(?) -phosphonous acid.** XII. Crystals, m. 125°. ⁸⁰
- 1,2,7,8-Dibenzoxanthene-9-phosphonous acid.** IG. Colorless solid (from EtOH); turns red in the air. ⁸⁹
- 2-Thiophenephosphonous acid.** XII. Needles, m. 70° (from water).²³⁸
- 4,4'-Biphenyldiphosphonous acid.** XXIII. Plates, m. 167° (from water).²²⁷

PHOSPHONIC ACIDS

PRIMARY PHOSPHONIC ACIDS

HYDROCARBON DERIVATIVES

- MePO(OH)₂.** V (traces). ⁴¹ X.¹⁰³ XIV.^{194, 222} Hygroscopic crystals, m. 104°, ²²² m. 105°. ¹⁰³ pK₁ 2.35; pK₂ 7.1. ²³⁷
- Dimethyl ester. IA.⁵ ID.²¹² Oil, b. 181°, ⁵ b₁₂ 67°, n_D²⁰ 1.4105, d₄²⁰ 1.1741. ³⁸

Diethyl ester. IA.^{5, 88, 194} IB.²²² Oil, b. 192–4°,⁵ b₁₀ 90°,²²² b₁ 64°,⁸⁸ b₁₁ 80.5–81°,²³ d₀¹ 1.0726,⁵ d₀¹ 1.0725,²³ d₀²³ 1.0508,⁵ n_D¹⁴ 1.4062,²³ n_D¹⁶ 1.4120.⁸⁸
 Dipropyl ester. Modified IA (from methyl iodide and sodio (C)-tetraethyl-(P)-dipropyl phosphonomalonate).²³ Oil, b₁₂ 105–6°, d₀¹ 1.0683, n_D¹⁸ 1.4082.²³
 Di-isopropyl ester. IA.⁸⁸ Oil, b₃ 66°, n_D^{16, 5} 1.4120.⁸⁸
 Diphenyl ester. IA.^{5, 194, 243} Crystals, m. 35°,²⁴³ m. 36–7°,¹⁹⁴ b₁₃ 205°,²⁴³ b₁₁ 190–5°,¹⁹⁴ b₁₁ 201–2°,⁵ supercooled: d₀¹ 1.2207, d₀²⁰ 1.2051.⁵
 Di-*p*-chlorophenyl ester. IA. Oil, b₂₀ 245°.¹⁹⁴
 Di-*m*-tolyl ester. IA. Oil, b₇ 200–5°.¹⁹⁴
 Di-*p*-tolyl ester. IA.¹⁹⁴ Oil, b₁₂ 220–5°.¹⁹⁴
 Dipseudocumenyl ester. IA.¹⁹⁴ Crystals, m. 79–90°.¹⁹⁴
o-Phenylene ester (cyclic). IA. Hygroscopic crystals, m. 80°.³⁴

The following esters of methanephosphonic acid are listed without a description of the methods of preparation.⁴⁹

Ethyl (enol acetoacetate); b₁ 130°.
 Ethyl *p*-nitrophenyl; b_{1, 5} 178°.
 Ethyl *o*-nitrophenyl; b_{1, 5} 157°.
 Ethyl phenyl; b₂ 136°.
 Ethyl *o*-chlorophenyl; b₁ 120°.
 Ethyl *o*-nitro-*p*-tolyl; b₂ 167°.
 Ethyl *o*-formylphenyl; b₁ 143°.
 Ethyl *p*-formylphenyl; b_{1, 5} 158°.
 Ethyl *o*-carbethoxyphenyl; b₁ 150°.
 Ethyl *p*-carbethoxyphenyl; b₁ 168°.
 Propyl *p*-chlorophenyl; b₃ 162°.
 Propyl 2,4-dinitrophenyl; b₁ 160°.

EtPO(OH)₂. X.¹⁰³ XI.^{97, 182} XIII.⁹⁷ XIV.^{137, 189, 222} XVI.¹⁶¹ Hygroscopic crystals, m. 30–5°,¹⁶¹ m. 44°,¹⁰³ m. 61–2°,¹³⁷ m. 61.5–2.5°,²²² b₈ 330–40°.¹⁶¹ *pK*₁ 2.45; *pK*₂ 7.85.²³⁷

Diethyl ester. IA.^{5, 88, 239} IB.^{88, 189, 222} IE.¹⁰⁹ XV.¹⁸⁹ Oil, b₇₆₀ 198°,¹⁸⁹ b₇₆₀ 203°,²⁰ b₂₀ 90–5°,¹⁸⁹ b₁₆ 90–2°,²³⁹ b₁₂ 85°,³⁸ b₉ 86–8°,²²² b₂ 62°,⁸⁸ d₀²⁰³ 0.8373,²⁰ d₂₅²¹ 1.032,⁸⁸ d₀²¹ 1.025,¹⁸⁹ d₄²⁰ 1.0259,²⁰ d₀²⁰ 1.0272,³⁸ n_D²⁰ 1.4165,³⁸ n_D²⁰ 1.4163,³⁰ n_D¹⁸ 1.4172.⁸⁸
 Ethyl 2-bromoethyl ester. IA. Oil, b₁₁ 129–30°, d₀²⁰ 1.3726, n_D²⁰ 1.4610.³⁵
 Dibutyl ester. IB.¹³⁷ Oil, b₁₇ 137–9°, d₄²⁵ 0.9623, n_D²⁵ 1.4258.¹³⁷
 1-Methoxy-2,3-glyceryl ester (cyclic). IA. Oil, b₃ 140–1°. ³⁵
o-Phenylene ester (cyclic). Hygroscopic crystals. IA. m. 69–70°. ³⁴

CH₂:CHPO(OH)₂. Free acid not isolated.

Diethyl ester. From the 2-chloroethyl (or 2-bromoethyl) derivative on treatment with alcoholic KOH,^{110, 145} diethylamine,¹⁴⁵ or triethylamine.⁸⁸ Liquid, b₃ 68–70°,¹¹⁰ b_{2, 5} 63°,⁸⁸ b₁ 50°,¹⁴⁵ d₀²⁰ 1.0526,¹¹⁰ n_D¹⁵ 1.4320,⁸⁸ n_D²⁰ 1.4300,¹¹⁰ n_D²⁵ 1.4260.¹⁴⁵

Di-2-chloroethyl ester. From the 2-chloroethyl derivative and alcoholic KOH. Oil, b₄ 137–9°, d₄²⁰ 1.3182, n_D²⁰ 1.4772.¹¹⁰

PrPO(OH)₂. XI.⁹⁷ XIII.⁹⁷ XIV.²²² Scales, m. 66°,⁹⁷ m. 72.5–4.5°. ²²²

Diethyl ester. IA.⁵ IB.²²² Oil, b₉ 92–3°,²²² b_{8, 5} 86–8°,⁵ d₀¹ 1.0467, d₀¹⁹ 1.0291.⁵

Dipropyl ester. IA.⁵ IB.³⁸ ID.²¹² Oil, b₁₈ 126°,²¹² b₁₀ 119°,⁵ b_{9, 5} 114°,³⁸ d₀²⁰ 0.9776,³⁸ d₄²² 1.0324,²¹² n_D²⁰ 1.4245.³⁸

CH₂:CH·CH₂PO(OH)₂. XIV (from the 3-bromopropyl derivative). Oil.^{134, 244}

Diethyl ester. IA (from 1,2-dibromopropane).⁸⁸ Oil, b₂ 78–81°, n_D²¹ 1.4320.⁸⁸

150 ACID DERIVATIVES WITH CARBON TO PHOSPHORUS LINK

iso-PrPO(OH)₂. X.¹⁰⁴ XI.⁹⁷ XIII.⁹⁷ XVI.¹⁶¹ Waxy solid, m. 71°. ⁹⁷

CH₂:CMe·PO(OH)₂. XIII. Hygroscopic mass. ⁹⁸

Dimethyl ester. XV. Oil, b₁₋₂ 44-6°, n_D²⁰ 1.4340. ⁹⁸

Dibutyl ester. XV. Oil, b_{0.25} 86-7°, n_D²⁰ 1.4376. ⁹⁸

BuPO(OH)₂ XIV.^{16, 137} Scales, m. 101-3°, ¹⁶ m. 103.5-4.0° ¹³⁷ (from ligroin).

Diethyl ester. IA.⁸⁸ Oil, b₁ 74°, n_D¹⁷ 1.4244. ⁸⁸

Dibutyl ester. IA.¹⁶ IB.^{88, 137} Oil, b₂₀ 160-2°, ¹³⁷ b₁₀ 150-1°, ¹⁶ b_{9.8} 146.5°, d₀⁰ 0.9634, d₁₇⁰ 0.9520, ¹⁶ d₂₀⁰ 0.9427, ⁸⁸ d₄²⁵ 0.9462, ¹³⁷ n_D²⁵ 1.4302. ¹³⁷

CH₂:CH·CH:CHPO(OEt)₂. IA or IB, followed by treatment with alcoholic KOH.

II, followed by XV and treatment with alcoholic KOH. Oil, b₁₁ 117-24°, n_D²⁵ 1.4400. ¹³⁸

iso-BuPO(OH)₂. X.¹⁰⁴ XI.⁹⁷ XIII.⁹⁷ XIV.^{8, 19} Scales, m. 124° (hemi-hydrate isolated only). ^{8, 19}

Di-isobutyl ester. IA.¹⁹ Oil, b. 258-9°, b₁₀ 133.5-4°, d₀⁰ 0.9629, d₄⁰ 0.9628, d₄²⁰ 0.9459, d₂₀²⁰ 0.9475. ^{8, 19}

Me₂C:CH·PO(OH)₂. Acid unreported in free state.

Di-allyl ester. XV. Oil, b₃₋₄ 110-5°, n_D²⁶ 1.4666. ²⁶⁰

Di-methallyl ester. XV. Oil, b₁₋₂ 110-20°, n_D²⁶ 1.4667. ²⁵⁰

AmPO(OH)₂. XIV. Scales, m. 120.5-1.5° (from ligroin). ¹³⁷

Diethyl ester. IA. Oil, b_{1.5} 86°, n_D^{15.5} 1.4282. ⁸⁸

Dibutyl ester. IB. Oil, b₁₇ 167-9°, d₄²⁵ 0.9428, n_D²⁵ 1.4318. ¹³⁷

Dibutyl isoprenephosphonate. Probably isomer mixture, from II, followed by XV and an alcoholic KOH treatment. Oil, b₁₅ 170-2°, n_D²⁵ 1.4510. ¹³⁸

iso-AmPO(OH)₂. X.^{40, 97, 104} XIII.⁹⁷ XX.⁹⁷ Plates, m. 139°, ⁴⁰ m. 160°, ¹⁰⁴ m. 166°. ⁹⁷

Diethyl ester. IA.⁸⁸ Oil, b_{0.8} 75°, n_D^{16.5} 1.4266. ⁸⁸

Diphenyl ester. XV. Heavy oil. ⁹⁷

n-C₆H₁₃PO(OH)₂. XIV. Scales, m. 104.5-6° (from ligroin); ¹³⁷ pK₁ 2.6; pK₂ 7.9. ²³⁷

Diethyl ester. IA. Oil, b₁₇ 140-5°, ¹³⁷ b₂ 103°, n_D¹⁷ 1.4311. ⁸⁸

Dibutyl ester. IB. Oil, b₂₀ 182-4°, d₄²⁵ 0.9366, n_D²⁵ 1.4332. ¹³⁷

n-C₇H₁₅PO(OH)₂. XIV.¹³⁷ By reduction of the 1-hydroxy derivative with HI at 200°. ⁹⁰ Scales, m. 106°, ⁹⁰ m. 103-3.5° (from ligroin). ¹³⁷

Diethyl ester. IA.⁸⁸ Oil, b_{1.9} 113°, n_D^{16.5} 1.4325. ⁸⁸

Dibutyl ester. IB.¹³⁷ Oil, b₁₇ 188-90°, d₄²⁵ 0.9313, n_D²⁵ 1.4355. ¹³⁷

n-C₈H₁₇PO(OH)₂. XIV. Scales, m. 99.5-100.5° (from ligroin). ¹³⁷

Diethyl ester. IA.⁸⁸ Oil, b_{1.2} 119°, n_D¹⁶ 1.4360. ⁸⁸

Dibutyl ester. IB.¹³⁷ Oil, b₂ 147-8°, d₄²⁵ 0.9262, n_D²⁵ 1.4370. ¹³⁷

Me₃C·CH₂·CMe:CHPO(OH)₂. II. Plates, m. 104-5° (from Et₂O-ligroin). ¹⁴⁸

Diallyl ester. XV. Oil, b₃₋₄ 135-40°, n_D²⁶ 1.4662. ²⁶⁰

Dimethallyl ester. XV. Oil, b₁ 110-22°, n_D²⁴ 1.4668. ²⁶⁰

n-C₉H₁₉PO(OH)₂. XIV. Scales, m. 99-100° (from ligroin). ¹³⁷

Diethyl ester. IA.¹³⁷ Oil, b₁₇ 177-86°. ¹³⁷

Dibutyl ester. IB. Oil, b₂ 159-61°, n_D²⁵ 1.4391, d₄²⁵ 0.9253. ¹³⁷

n-C₁₀H₂₁PO(OH)₂. XIV. Scales, m. 102-2.5° (from ligroin). ¹³⁷

Diethyl ester. IA. Oil, b₁₇ 186-93°. ¹³⁷

Dibutyl ester. IB. Oil, b₁ 161°, d₄²⁵ 0.9232, n_D²⁵ 1.4402. ¹³⁷

n-C₁₂H₂₅PO(OH)₂. XIV. Scales, m. 100.5-1.5° (from ligroin); ¹³⁷ pK₁ - ; pK₂ 8.25. ²³⁷

Diethyl ester. IA.^{88, 94, 137} Oil, b₁ 160°, ⁸⁸ b_{1.2} 164-5°, ⁹⁴ b₃ 165-75°, ¹³⁷ n_D²⁵ 1.4389, ⁹⁴ n_D^{15.5} 1.4419. ⁸⁸

Dibutyl ester. IB. Oil, b₈ 196-9°, d₄²⁵ 0.9153, n_D²⁵ 1.4432. ¹³⁷

- n*-C₁₄H₂₉PO(OH)₂.** XIV. Scales, m. 97–8° (from ligroin).¹³⁷
 Diethyl ester. IA.¹³⁷ Oil, b₃ about 200°. ¹³⁷
 Dibutyl ester. IB. Oil, b₃ 217–9°, *d*₄²⁵ 0.9114, *n*_D²⁵ 1.4460.¹³⁷
- n*-C₁₆H₃₃PO(OH)₂.** XIV. Scales, m. 94.5–5.5° (from ligroin).¹³⁷
 Dibutyl ester. IB. Oil, b₂ 226–8°, *d*₄²⁵ 0.9090, *n*_D²⁵ 1.4481.¹³⁷
- n*-C₁₈H₃₇PO(OH)₂.** XIV. Scales, m. 98.5–99° (from ligroin).¹³⁷
 Dibutyl ester. IB. Oil, b₂ 248–50°, *d*₄²⁵ 0.9037, *n*_D²⁵ 1.4499.¹³⁷
- n*-C₁₆H₃₃CH:C(PO₃H₂)C₁₇H₃₅-*n*.** By dehydration of the 18-hydroxy derivative at 120–40°. Solid, m. 35–40°. ⁹⁸
- PhCH₂PO(OH)₂.** IVA.¹⁵⁵ XIII.¹⁵¹ XIV.^{34, 139} Prisms, m. 166°, ^{139, 155} m. 169°, ¹⁵¹ m. 169–70° (from AcOH).³⁴ Soluble in water. On heating with phosphorous acid the substance appears to yield benzylphosphine.¹⁵¹
 Diethyl ester. IA.²³⁹ IB.²³⁹ Oil, b₂₅ 169–71°, b₁₄ 155°. ²³⁹
 Ethyl 2-chloroethyl ester. IA. Oil, b_{7.5} 182–3°, *n*_D²⁰ 1.5128. ³⁵
 Dibutyl ester. IB. Oil, b₄ 140–3°, *n*_D²⁵ 1.4820. ¹³⁹
 Diphenyl ester. IA. Crystals, m. 61–2° (from ligroin).¹⁹⁴
 1-Methoxy-2,3-glyceryl ester (cyclic). IA. Crystals, m. 88–9°. ³⁵
 1-Ethoxy-2,3-glyceryl ester (cyclic). IA. Oil, b₂ 198–9°. ³⁵
 1-Chloro-2,3-propylene ester (cyclic). IA. Crystals, m. 94–5°. ³⁵
o-Phenylene ester (cyclic). IA. Obtained only in crude state. ³⁴
- 4-O₂NC₆H₄CH₂PO(OH)₂.** By nitration of the above acid with cold, fuming nitric acid. Yellow needles, dec. 217°. ¹⁴⁵
- 4-H₂NC₆H₄CH₂PO(OH)₂.** By reduction of the nitro derivative (above) with aqueous sodium sulfide. Yellowish powder, dec. 323–5°, very sparingly soluble in water. ¹⁴²
- 2-HO-5-O₂NC₆H₃CH₂PO(OH)₂.** XIV. Crystals, m. 224–9°. ¹⁵⁶
 Diethyl ester. IA. Solid, m. 137°. ¹⁵⁶
- 2-MeO-5-OHC·C₆H₃CH₂PO(OH)₂.** Free acid unreported.
 Diethyl ester. IA. Oil, b₂ 184–6°, *d*₂₀²⁰ 1.1921, *n*_D²⁰ 1.5280. Phenylhydrazone, m. 117°. ¹⁵⁶
- 4-MeC₆H₄CH₂PO(OH)₂.** XIV.^{139, 156} Plates, m. 185°, ¹³⁹ m. 185–6°. ¹⁵⁶
 Diethyl ester. IA.¹⁵⁶ Oil, b₂ 160–3°, *d*₂₀²⁰ 1.0832, *n*_D²⁰ 1.4958. ¹⁵⁶
 Dibutyl ester. IB.¹³⁹ Oil, b₂₀ 213–5°, *n*_D²⁵ 1.4852. ¹³⁹
- 4-EtC₆H₄CH₂PO(OH)₂.** XIV. Needles, m. 178–8.5° (from water).¹³⁹
 Diethyl ester. IA. Oil, b₁₄ 176–8°. ¹³⁹
 Dibutyl ester. IB.¹³⁹ Oil, b₃ 147–50°, *n*_D²⁵ 1.4845. ¹³⁹
- 2,4-Me₂C₆H₃CH₂PO(OH)₂.** XIV. Crystals, m. 184–6°. ¹⁵⁶
 Diethyl ester. IA. Oil, b₂ 130–2°, *d*₂₀²⁰ 1.0708, *n*_D²⁰ 1.4990. ¹⁵⁶
- 2-Me-5-iso-Pr·C₆H₃CH₂PO(OH)₂.** XIV. Crystals, m. 175–7°. ¹⁵⁶
 Diethyl ester. IA. Oil, b₂ 146–8°, *d*₂₀²⁰ 1.0420, *n*_D²⁰ 1.4940. ¹⁵⁶
- 4-BuC₆H₄CH₂PO(OH)₂.** XIV. Needles, m. 162–3° (from ligroin).¹³⁹
 Dibutyl ester. IB. Oil, b₂ 175–8°. ¹³⁹
- 1-C₁₀H₇CH₂PO(OH)₂.** XIV. Plates, m. 212–12.5° (from water).¹³⁹
 Diethyl ester. IA. Oil, b₅ 205–6°, *n*_D²⁵ 1.5610. ¹³⁹
- (3,4-Tetramethylenephényl)methane phosphonic acid.** XIV. Solid, m. 165°. ¹⁴⁶
 Diethyl ester. IA. Oil, b₃ 165–7°, *d*₂₀²⁰ 1.1063, *n*_D²⁰ 1.5165. ¹⁴⁶
- 4-PhC₆H₄CH₂PO(OH)₂.** XIV. Crystals, dec. 250° (from water).¹³⁹
 Dibutyl ester. IB. Undistillable oil. ¹³⁹

9-Phenanthrylmethanephosphonic acid. XIV. Plates, dec. 212° (from alcohol-benzene-ligroin).¹³⁹

Dibutyl ester. IB. Undistillable oil.¹³⁹

(PhCH₂)₂CHPO(OH)₂. Modified IVA (heating dibenzyl ketone with red phosphorus and conc. HI for 6 hr. at 180°).¹⁹¹ Needles, m. 142° (from water). Aniline salt, m. 126° (from EtOH); phenylhydrazine salt, m. $148-9^{\circ}$.¹⁹¹

Diethyl ester. XV. Oil, b₂₀ 240° .¹⁹¹

Diphenyl ester. XV. Prisms, m. 120° (from EtOH).¹⁹¹

2-Indenephosphonic acid. II.^{44, 246} Needles, m. 184° (from AcOH).⁴⁴ On hydrogenation in the presence of palladium in propanol it yields 2-dihydroindenephosphonic acid, prisms, m. 196° (from AcOH).⁴⁴ Heating the indene derivative in alcohol in the presence of sodium ethoxide with aldehydes yields the corresponding condensation products: 1-benzylidene-2-indenephosphonic acid, m. $188-9^{\circ}$, 1-anisylidene analog, m. 192° , and 1-piperonylidene analog, m. 194° .^{44, 246}

Camphenephosphonic acid. II. Exists in two, apparently stereoisomeric, forms: insoluble in ether, m. 184° (sesquihydrate), and soluble in ether, dec. 167° .¹⁷⁶

6-Chloro-8-(diethyl phosphonomethyl)-1,3-benzodioxane. IA. Oil, b₃ $195-8^{\circ}$, d_{20}^{20} 1.2892, n_D^{20} 1.5230.¹⁶⁶

2-Thienylmethanephosphonic acid. XIV. Plates, m. $108-9^{\circ}$ (from water).¹⁴³

Dibutyl ester. IB. Oil, b₃ $147-50^{\circ}$.¹⁴³

Cyclohexanephosphonic acid. XIII. Crystals, m. $166-7^{\circ}$ (from water).⁶²

Ph₃CPO(OH)₂. IC.¹¹ XI (best with KMnO₄ or with iodine in AcOH).⁹⁹ XIII.^{11, 54, 56} XIV.^{10, 11} Prisms, m. 237° ,⁵⁴ m. 279° ,^{10, 11} m. $283-3.5^{\circ}$.⁹⁹ (from AcOH or benzene).

Dimethyl ester. IA.¹¹ IB.¹⁰ From the free acid, Me₂SO₄ and K₂CO₃ in hot toluene.⁹⁹ Colorless crystals, m. $154.5-5.5^{\circ}$,⁹⁹ m. $157-8^{\circ}$,¹⁰ the older report of two apparently isomeric forms: colorless, m. $157-8^{\circ}$, and yellow, m. $158-9^{\circ}$, appears to be in error.⁹⁹

Monoethyl ester. XV combined with XIII.⁹⁹ Crystals, m. 259° (from benzene).⁹⁹

Diethyl ester. IA.¹¹ IB.^{10, 13} XV.⁹⁹ XXI.⁹⁹ Crystals, m. $120-1^{\circ}$,^{10, 11} m. $121-2^{\circ}$.⁹⁹

Dipropyl ester. IA.¹¹ IB.¹⁰ Crystals, m. $109-10^{\circ}$ (from benzene-ligroin).^{10, 11}

Di-isopropyl ester. IA.¹¹ Three forms are claimed: colorless, m. $122.5-3.0^{\circ}$, and m. $216.5-17.0^{\circ}$, and yellow, m. $119-20^{\circ}$.¹¹

Di-isobutyl ester. IA.^{10, 11} IB.¹⁰ Colorless, m. $96-6.5^{\circ}$.^{10, 11}

1,3-Butanediol ester (cyclic). IA. Crystals, m. $192-3^{\circ}$.³⁵

Ethyl 2-bromoethyl ester. IA. Crystals, m. $99-101^{\circ}$.³⁵

Methyl 2-bromoethyl ester. IA. Crystals, m. $153-5^{\circ}$.³⁵

Ph₂(4-ClC₆H₄)CPO(OH)₂. IC.⁵⁵ Crystals, m. 273° (from AcOH).⁵⁵

Ph₂(4-BrC₆H₄)CPO(OH)₂. IC.⁵⁵ Crystals, m. 297° (from AcOH).⁵⁵

Ph₂(4-MeOC₆H₄)CPO(OH)₂. IC.⁵⁵ Crystals, m. 210° (from AcOH).⁵⁵

Ph₂(3-HOC₆H₄)CPO(OH)₂. IC and XIII (from the methoxy derivative).⁵⁵ Crystals (dihydrate), m. 248° ; benzoate, m. $235-7^{\circ}$.⁵⁵ On being warmed with Me₂SO₄ in the presence of alkali, this acid yields the corresponding methoxy derivative, m. 197° (from AcOH).⁵⁵

Ph₂(4-MeC₆H₄)CPO(OH)₂. IC.⁵⁵ Crystals, m. 254° (from benzene).⁵⁵

Ph₂(1-C₁₀H₇)CPO(OH)₂. IC.⁵⁵ Crystals, m. 256° (from EtOH).⁵⁵

Ph₂(2-C₁₀H₇)CPO(OH)₂. IC.⁵⁵ Crystals, m. 247.5° (from AcOH).⁵⁵

Ph₂(4-PhC₆H₄)CPO(OH)₂. XIII. Needles, m. 270–2°. ²⁷Dimethyl ester. IA. Crystals, m. 124–5°. ²⁸Diethyl ester. IA. ²⁸ XV. ²⁸ Crystals, m. 147–8°, ²⁸ m. 145–6°. ²⁹Dipropyl ester. IA. ²⁸ XV. ²⁹ Crystals, m. 131–3°, ²⁸ m. 131–2°. ²⁹Di-isopropyl ester. IA. Crystals, m. 196.5–9.5°. ²⁸Dibutyl ester. IA. ²⁸ Crystals, m. 90–1°. ²⁸ XV. ²⁹ Crystals, m. 90–1°. ²⁹Di-isobutyl ester. IA. ²⁸ XV. ²⁹ Crystals, m. 93–4°. ^{28, 29}o-Phenylene ester (cyclic). XV. Crystals, m. 163–4° (from Bu₂O). ²⁷**Ph(4-PhC₆H₄)₂CPO(OH)₂. XIII.** Needles, m. 164–5°. ²⁷Dimethyl ester. IA. Crystals, m. 159°. ²⁸Diethyl ester. IA. ²⁸ XV. ²⁹ Crystals, m. 140–1°, ²⁸ m. 139–41°. ²⁹Dipropyl ester. IA. ²⁸ Crystals, m. 110–1°. ²⁸Di-isopropyl ester. IA. ²⁸ Crystals, m. 159–60°. ²⁸Dibutyl ester. IA. ²⁸ Crystals, m. 88–9°. ²⁸Di-isobutyl ester. IA. ²⁸ XV. ²⁹ Crystals, m. 118–20°. ^{28, 29}o-Phenylene ester (cyclic). XV. Crystals, m. 74–88°. ²⁷**(4-PhC₆H₄)₃CPO(OH)₂. XIII.** ²⁷ XIV. ²⁸ Crystals, m. 292–4°. ²⁷Dimethyl ester. IA. ²⁸ Crystals, m. 200–1°. ²⁸Diethyl ester. IA. ²⁸ XV. ²⁹ Crystals, m. 144–5°, ²⁸ m. 143–5°. ²⁹Dipropyl ester. IA. ²⁸ Crystals, m. 148–9°. ²⁸Di-isopropyl ester. IA. ²⁸ Crystals, m. 177–8°. ²⁸Dibutyl ester. IA. ²⁸ Crystals, m. 132–3°. ²⁸ XV. ²⁹ Crystals, m. 130–2°. ²⁹Di-isobutyl ester. IA. ²⁸ Crystals, m. 120–1°. ²⁸o-Phenylene ester. XV. Crystals, m. 212–4°. ²⁷

PhC(PO₃H₂):CH₂. IVB (by-product). ⁷³ By heating Ph·CCl(PO₃H₂)Me to 180–90° or by long boiling in hydrochloric acid. ⁷⁰ Crystals, m. 112–3° (from Et₂O·CHCl₃). Aniline salt, m. 180–1°. ⁷³ Long heating with hydrobromic acid to 100° yields some very crude 2-bromo-1-phenylethanephosphonic acid, m. 110–40°. ⁷⁰

PhCH:CH·PO(OH)₂. II. ^{44, 148, 246} Plates, m. 154.5–55° (from water); ¹⁴⁸ forms two stereoisomers: m. 146° and m. 150°, ⁴⁴ which after crystallization from ethylene bromide, m. 146°. ⁴⁴ Acid sodium salt, plates, m. 224–7° (from water). ¹⁴⁸

Dimethallyl ester. XV. Oil, b₂ 158–64°, n_D²⁵ 1.5391. ²⁶⁰Diallyl ester. XV. Oil, b₁ 152–8° (must be distilled with copper inhibitor), n_D²⁶ 1.5442. ²⁵⁰Hydrogenation of the free acid yields **phenylethanephosphonic acid**, m. 137–8°. ⁴⁴

PhC: CPO(OH)₂. By treatment of PhCCl:CHPO(OH)₂ with potassium hydroxide. Crystals, m. 142°. ⁴⁶

PhMeC:CH·PO(OH)₂. II. Crystals, m. 95° (from Et₂O). ⁴⁴ The saturated analog, obtained by hydrogenation, is an oil. ⁴⁴

3-ClC₆H₄CH:CH·PO(OH)₂. II. Crystals, m. 168°. ⁴⁶

2-ClC₆H₄C: CPO(OH)₂. By treatment of RCCl:CH·PO(OH)₂ with potassium hydroxide. Crystals, m. 134°. ⁴⁶

2,4-Me₂C₆H₃CH:CH·PO(OH)₂. II. Crystals, m. 142–3° (from water). ¹⁴⁸

2,4,6-Me₃C₆H₂CH:CH·PO(OH)₂. II. Crystals, m. 176–8° (from dil. EtOH). ¹⁴⁸

4-EtC₆H₄CH:CH·PO(OH)₂. II. Crystals, m. 138–40° (from EtPh). ¹⁴⁸

2-tert-BuC₆H₄CH:CH·PO(OH)₂. II. Crystals, m. 188–9° (from water). ¹⁴⁸

4-tert-BuC₆H₄CH:CHPO(OH)₂. II. Crystals, m. 150.5–1.5° (from dil. EtOH). ¹⁴⁸

2-PhC₆H₄CH:CH·PO(OH)₂. II. Crystals, m. 186–8° (from water). ¹⁴⁸

3-PhC₆H₄CH:CH·PO(OH)₂. II. Crystals, m. 156–7.5°. ¹⁴⁸

4-PhC₆H₄CH:CH·PO(OH)₂. II. Crystals, m. 193–3.5° (from BuOH). ¹⁴⁸

154 ACID DERIVATIVES WITH CARBON TO PHOSPHORUS LINK

- 2-C₁₀H₇CH:CH·PO(OH)₂.** II. Crystals, m. 181.5–82° (from AcOH).¹⁴⁸
Ph₂C:CH·PO(OH)₂. II. Crystals, m. 167° (from xylene).⁴⁴
Ph₂CH·CH₂·PO(OH)₂. By hydrogenation of the above compound in the presence of palladium. Crystals, m. 213°. ⁴⁴
(2-FC₆H₄)PhC:CH·PO(OH)₂. II. Crystals, m. 180°. ⁴⁵
(4-ClC₆H₄)PhC:CH·PO(OH)₂. II. Crystals, m. 181°. ⁴⁵
(4-ClC₆H₄)₂C:CH·PO(OH)₂. II. Crystals, m. 158–9°. ⁴⁵
(4-MeOC₆H₄)PhC:CH·PO(OH)₂. II. Crystals, m. 145°. ⁴⁵
(4-MeOC₆H₄)PhCHCH₂PO(OH)₂. By hydrogenation of the above compound in the presence of palladium. Crystals, m. 102–3°. ⁴⁵
(4-ClC₆H₄)(4-MeOC₆H₄)C:CH·PO(OH)₂. II. Crystals, m. 132–3°. ⁴⁵
(4-ClC₆H₄)(4-MeOC₆H₄)CHCH₂PO(OH)₂. By hydrogenation of the above compound in the presence of palladium. Crystals, m. 126–7°. ⁴⁵
(2-MeC₆H₄)PhC:CH·PO(OH)₂. II. Crystals, m. 154°. ⁴⁷
(2-MeC₆H₄)PhCHCH₂PO(OH)₂. By hydrogenation of the above compound in the presence of palladium. Crystals, m. 160–1°. ⁴⁷
(4-PhC₆H₄)PhC:CH·PO(OH)₂. II. Crystals, m. 201°. ⁴⁵
(4-PhC₆H₄)PhCHCH₂PO(OH)₂. By hydrogenation of the above compound in the presence of palladium. Crystals, m. 236°. ⁴⁵
(4-PhC₆H₄)(4-MeC₆H₄)C:CH·PO(OH)₂. II. Amorphous solid. ⁴⁵
(1-C₁₀H₇)PhC:CH·PO(OH)₂. II. Crystals, m. 188°. ⁴⁷
(2-C₁₀H₇)PhC:CH·PO(OH)₂. II. Crystals, m. 220°. ⁴⁷
2-(2-Fluorenyl)ethenephosphonic acid. II. Crystals, dec. 200–5° (from EtOH-PrOH).¹⁴⁸
9,9-Diphenyl-9,10-dihydroanthracyl-10-methylenephosphonic acid. II. Unstable solid, m. 205°. ⁴⁷
PhCH₂CH₂CH(PO₃H₂)Ph. By hydrogenation of monoalkyl esters of the acid, PhCOCH₂CH(PO₃H₂)Ph, in the presence of platinum. Crystals, m. 168–71° (from cyclohexane).⁸⁸
PhCH:CH·CH:CH·PO(OH)₂. II. Crystals, m. 192°. ^{45, 148}
PhCH₂CH₂CH₂CH₂PO(OH)₂. By hydrogenation of the above compound in the presence of palladium. Crystals, m. 95°. ⁴⁵

HALOGENATED DERIVATIVES

- FCH₂PO(OCHMeEt)₂.** XXV. Oil, b₃ 96–100°. ²²⁰
ICH₂PO(OEt)₂. IA. Oil, b₆ 133°, ²⁶ b_{0.7} 101°, ⁸⁸ d₀⁰ 1.691, d₀¹⁹ 1.6662, ²⁸ n_D¹⁷ 1.4975. ⁸⁸
Cl₃CPO(OMe)₂. IA. ^{134, 137} Oil, b₁₂ 121–2°, b₉ 110–2°, ¹³⁷ b_{7–10} 110–2°, ¹³⁴ d₀⁰ 1.4840, d₀¹⁵ 1.4594. ¹³⁷
Cl₃CPO(OEt)₂. IA. ^{134, 137, 141} Oil, b₁₆ 135–7°, ¹⁴¹ b₁₆ 129–30.5°, ¹³⁷ b₁₃ 127–8°, ¹⁴¹ b₁₂ 122–3°, ¹³⁷ b_{7–10} 122–3°, ¹³⁴ d₀⁰ 1.3829, d₀⁴ 1.3664, ¹³⁷ n_D²⁵ 1.4582, ¹⁴¹ n_D¹⁴ 1.4585. ¹³⁷
Cl₃CPO(OCH₂CH:CH₂)₂. IA. ^{134, 137} Oil, b₁₀ 136–8°, ¹³⁷ b_{7–10} 136–8°, ¹³⁴ d₀⁰ 1.1719, d₀²⁰ 1.500, ¹³⁷ n_D²⁰ 1.4552. ¹³⁷
Cl₃CPO(OPr)₂. IA. ^{134, 137} Oil, b₁₂ 144–5°, ¹³⁷ b_{7–10} 145°, ¹³⁴ d₀⁰ 1.2603, d₀¹⁵ 1.2459, n_D¹⁵ 1.4582. ¹³⁷
Cl₃CPO(OPr-iso)₂. IA. ^{134, 137} Oil, b₁₂ 127–30°, ¹³⁷ b_{7–10} 127–30°, ¹³⁴ d₀⁰ 1.2350, d₀²² 1.2206, n_D²⁰ 1.4478. ¹³⁷
Cl₃CPO(OBu)₂. IA. ^{134, 137, 141} Oil, b_{7–10} 145–6°, ¹³⁴ b₇ 145–6°, ¹³⁷ b₆ 150–5°, ¹⁴¹ d₀⁰ 1.1814, d₀¹⁷ 1.1679, n_D¹³ 1.4521, ¹³⁷ n_D²⁵ 1.4490. ¹⁴¹
Cl₃CPO(OBu-iso)₂. IA. ^{134, 137} Oil, b₉ 144–5°, ¹³⁷ b_{7–10} 144–5°, ¹³⁴ d₀⁰ 1.2114, d₀¹⁷ 1.1942, n_D¹⁵ 1.4487. ¹³⁷
FCH₂CH₂PO(OEt)₂. IA. ²²⁰ IB. ²²⁰ Oil, b₁₁ 74–5°, b₁₈ 86.5–88°. ²²⁰

- $\text{ClCH}_2\text{CH}_2\text{PO}(\text{OH})_2$.** XIII.¹¹⁴ XIV.¹¹⁴ Needles, m. 74–5° (from benzene).¹¹⁴
 Dimethyl ester. XV. Oil, b_1 65–7°, d_4^{20} 1.2666, n_D^{20} 1.4490.¹¹⁹
 Diethyl ester. IA (impure).¹¹⁸ XV.¹¹⁹ Oil, b_7 103–10°, b_4 92–4°, d_4^{20} 1.1558, n_D^{20} 1.4390.¹¹⁹
 Di-2-chloroethyl ester. IA.¹¹⁴ Crystals, m. 37°, b_8 170–2°, on supercooling: d_0^{26} 1.3906, d_4^{26} 1.3892, n_D^{26} 1.4828.¹¹⁴
 Diphenyl ester. XV. Oil, b_2 189–90°, b_1 176–8.6°, d_0^{15} 1.2671, d_4^{15} 1.2663, n_D^{15} 1.5577.¹¹⁹
o-Phenylene ester (cyclic). XV. Oil, $b_{4.5}$ 167–70°, d_0^{20} 1.4026, d_4^{20} 1.4015, n_D^{20} 1.5502.¹¹⁹
 Mono-(2-hydroxyphenyl) ester. XV. Needles, m. 100–2°.¹¹⁹
 $\text{Br-CH}_2\text{CH}_2\text{PO}(\text{OH})_2$. XIII. Plates, m. 86–7° (from benzene- $\text{C}_2\text{H}_4\text{Cl}_2$).¹¹⁸
 Diethyl ester. IA.^{88, 145} Oil, b_2 86–7°, $b_{0.8}$ 101°, $n_D^{16.5}$ 1.4600, n_D^{25} 1.4555.¹⁴⁵
 Di-2-bromoethyl ester. IA. Crystals, m. 48–9° (from ligroin), $b_{2.5}$ 190–1°.¹¹⁸
 $\text{BrCH}_2\cdot\text{CHBr}\cdot\text{PO}(\text{OEt})_2$. By addition of bromine to the vinyl compound. Oil, b_4 129–31.5°, d_4^{20} 1.6596, d_{20}^{20} 1.6634, n_D^{20} 1.4939.¹¹⁰
 $\text{Br}(\text{CH}_2)_3\text{PO}(\text{OH})_2$. XIV.¹⁸⁸ Plates, m. 107–8° (from water).¹⁸⁸
 Diethyl ester. IA.^{188, 294} Undistillable oil.
 $\text{NC}(\text{CH}_2)_3\text{PO}(\text{OEt})_2$. IB.²²¹ Oil, b_8 163–4°, d_4^{17} 1.0885.²²¹
 $\text{Me}_2\text{CCl}\cdot\text{CH}_2\text{PO}(\text{OH})_2$. II. Needles, m. 95–7°.⁴⁷
 $n\text{-C}_6\text{H}_{11}\text{Cl}\cdot\text{CH}\cdot\text{PO}(\text{OH})_2$. II. Oil.⁴⁶
 Diethyl ester. XXI. Oil, b_{17} 152°.⁴⁶
***iso*-Pr $\cdot\text{CH}_2\cdot\text{CHCl}\cdot\text{PO}(\text{OH})_2$.** XIII. Colorless solid.⁹⁰
 Diethyl ester. XV. Undistillable oil.⁹⁰
PhMeCCl $\cdot\text{PO}(\text{OH})_2$. IVB, best by saturation of the reaction mixture of AcPh, PCl_3 , and AcOH with dry hydrogen chloride. Needles, m. 174–5° (from ether).⁷⁰
 $\text{ClCH}_2\text{CClPh}\cdot\text{PO}(\text{OH})_2$. By addition of chlorine to the vinyl compound. Crystals, m. 175–8°.⁷⁰
 $\text{Br-CH}_2\text{CBrPh}\cdot\text{PO}(\text{OH})_2$. By addition of bromine to the vinyl compound. Crystals, m. 186–8° (from $\text{Et}_2\text{O-CHCl}_3$).⁷⁰
 $\text{BrCH}\cdot\text{CPh}\cdot\text{PO}(\text{OH})_2$. By heating the above compound above its melting point in vacuum. Crystals, m. 133–5° (from CCl_4).⁷⁰
 $(2\text{-ClC}_6\text{H}_4)\text{CCl}\cdot\text{CH}\cdot\text{PO}(\text{OH})_2$. II. Crystals, m. 187°.⁴⁶
 $(2\text{-MeOC}_6\text{H}_4)\text{CCl}\cdot\text{CH}\cdot\text{PO}(\text{OH})_2$. II. Crystals, m. 64–7° (monohydrate), m. 125–7° (anhydrous).⁴⁶
 $(4\text{-MeOC}_6\text{H}_4)\text{CCl}\cdot\text{CH}\cdot\text{PO}(\text{OH})_2$. II. Crystals, m. 105°.⁴⁶
PhCH $_2\cdot\text{CCl}\cdot\text{CH}\cdot\text{PO}(\text{OH})_2$. II (from methylphenylacetylene). Needles, m. 179°, along with an isomer, m. 154°.⁴⁶
Chlorofenchenephosphonic acid. XVII (from *d*-fenchone). Plates, m. 196° (from Me_2CO).⁹¹

AMINO SUBSTITUTED DERIVATIVES

- $\text{H}_2\text{NCH}_2\text{PO}(\text{OH})_2$.** IB (from dibutyl sodiophosphite and bromomethylphthalimide, followed by hydrolysis with conc. HBr).⁹⁰ IC (from methylolacetamide, followed by hydrolysis with conc. HCl; ^{84, 89} from $\text{RCO}\cdot\text{NHCH}_2\text{PO}(\text{OH})_2$ by hydrolysis with HCl ^{84, 225}). Crystals, m. over 300° (from water); only moderately soluble in cold water.^{84, 89, 85, 225} pK_1 1.85; pK_2 5.35; pK_3 10.0.⁸⁹ Crude product is also described.²²⁷
 $n\text{-C}_{17}\text{H}_{35}\text{CO}\cdot\text{NHCH}_2\text{PO}(\text{OH})_2$. IC (using AcOH catalyst). Crystals, sinter at 108° (from EtOH).⁸⁵

PhCO·NHCH₂PO(OH)₂. IC (using AcOH catalyst). Crystals, m. 182° (from dil. Me₂CO).⁸⁵

MeNHCH₂PO(OH)₂. IC (by hydrolysis of RCO·NMe·CH₂PO(OH)₂ with 5% HCl). Crystals, m. over 240° (from dil. MeOH).²²⁵

n-C₁₇H₃₅CO·NMe·CH₂PO(OH)₂. IC (using AcOH catalyst). A waxy solid.⁸⁵

H₂NCH₂CH₂PO(OH)₂. XIV-IA (from triethyl phosphite and bromoethylphthalimide, followed by hydrolysis with conc. HBr).¹⁴² XIV-IB (as above, using dibutyl sodiophosphite).⁸⁸ By Hofmann reaction from H₂NCO·CH₂CH₂PO(OEt)₂, followed by XIV.⁸⁷ Needles, resinify at 265°, m. 285°,¹⁴² m. 281–2° (from 50% EtOH),⁸⁷ dec. 250° (from water).⁵⁸ *pK*₁ 2.45; *pK*₂ 7.0; *pK*₃ 10.8.²³⁷

Dibutyl ester. IB (from BrCH₂CH₂NH₂·HBr). Oil, *b*₂₅ 134–5°.⁸⁸

Et₂NCH₂CH₂PO(OEt)₂. From the 2-chloroethyl derivative and aqueous Et₂NH. Yellow oil, *b*₃ 106–7°, *n*_D²⁵ 1.4380; methiodide, m. 104–6°.¹⁴⁵

Bu₂NCH₂CH₂PO(OEt)₂. Prepared as above, using Bu₂NH. Yellow oil, *b*₃ 140–2°, *n*_D²⁵ 1.4421.¹⁴⁵

Ph₂N·C(PO₃H₂)(Me)Cl. XVII (low yield). Crystals, m. 225°.⁹²

H₂NCH₂CH₂CH₂PO(OH)₂. From the bromo derivative and aqueous NH₄OH at room temperature. Needles, m. 274° (from dil. EtOH).¹⁴²

PhNH·CH₂CH₂CH₂PO(OH)₂. From the bromo derivative and aniline at 125°. Colorless prisms, m. 129–30° (from water).^{136, 237} *pK*₁ 2.1; *pK*₂ 4.25; *pK*₃ 7.15.²³⁷ Mono sodium salt: plates, m. 187–9.5° (from water).¹³⁶

H₂N(CH₂)₄PO(OH)₂. XIV-IB (from bromobutylphthalimide and dibutyl sodiophosphite, followed by acid hydrolysis).^{58, 237} Crystals, m. 133–4°. *pK*₁ 2.55; *pK*₂ 7.55; *pK*₃ 10.9.²³⁷

H₂N(CH₂)₆PO(OH)₂. XIV-IB (as in the above preparation).⁵⁸ No m. is reported. *pK*₁ 2.6; *pK*₂ 7.6; *pK*₃ 11.0.²³⁷

H₂N(CH₂)₁₀PO(OH)₂. From HO₂C(CH₂)₁₀PO(OH)₂ and HN₃ at 45° in sulfuric acid. Crystals, m. 35–6° (from EtOH).⁵⁸ *pK*₁ -; *pK*₂ 8.0; *pK*₃ 11.25.²³⁷

PhCH(NH₂)PO(OH)₂. By reduction of *p*-nitrophenylhydrazones of diethyl benzoylphosphonate (best with aluminum amalgam),¹⁴⁴ followed by hydrolysis with hydrochloric acid.^{142, 144} Needles, m. 272–3° (from water).¹⁴⁴

PhMeC(NH₂)PO(OH)₂. From the chloro derivative and NH₄OH at room temperature. Flakes, m. 214–5°.¹⁴²

HYDROXY SUBSTITUTED DERIVATIVES

HOCH₂PO(OH)₂. IVB.²³³ XIV.²⁶ By hydrolysis of PhCH₂OCH₂PO(OEt)₂ at 120° with 10% HCl.² Hygroscopic crystals, m. 84–5°;² m. 84.5–6°;²⁶ m. 85°.²²³ Best crystallized from EtOH-AcOH; pyridine salt, m. 105°.²²³

Diethyl ester. IB (from CH₂I₂ in EtOH).²⁶ From the iodo derivative and diethyl potassium phosphite, in EtOH.²⁶ Oil, *b*₅ 72°, *d*₄²⁰ 1.0726.²⁶

PhCH₂OCH₂PO(OEt)₂. IA.² IB.² Oil, *b*₁₂ 180–3°, *b*₄ 169–70°, *d*₄²⁰ 1.120, *n*_D²⁰ 1.4930.²

PhCH₂OCH₂PO(OBu)₂. IB.² Oil, *b*₃ 168–70°, *d*₄²⁰ 1.034, *n*_D²⁰ 1.6589.²

HOCH₂CH₂PO(OH)₂. X. Isolated as a yellow, insoluble silver salt.¹²¹

Diethyl ester. IH. Oil, *b*₉ 120–30°.⁶¹

PhOCH₂CH₂PO(OH)₂. XIV. Needles, m. 130–1°.²¹¹

Diethyl ester. IA. Oil, *b*₁₀ 185–7°, *d*₄²⁰ 1.11, *n*_D²⁰ 1.5005.²¹¹

MeCHOH·PO(OH)₂. IVB. Crystals, m. 74–8°, dec. 100°.⁹⁰ Less satisfactorily prepared by IVA from paraldehyde^{160, 174} and by XI.¹⁶⁰

Me₂C(OH)PO(OH)₂. IVA.^{165, 166-7, 174} IVB.⁷³ XI.^{165, 166} Crystals, m. 175°, ¹⁶⁶ m. 167-9° (from AcOH).⁷³ Treatment with benzoyl chloride in pyridine yields the benzoate, m. 102° (from water).¹⁶⁷

Dimethyl ester. XXI. Crystals, m. 76°.^{167, 174}

Diethyl ester. XXI. Oil, m. 14-5°, b₂₀ 145°.^{167, 174}

Diphenyl ester. IVB. Crystals, m. 113-4° (from ligroin); acetate, m. 72-2.5°.⁷⁶

Me(ClCH₂)C(OH)PO(OH)₂. Free acid has not been reported.

Diphenyl ester. IVB. Cubic crystals, m. 119°.⁷⁶

EtCHOH·PO(OH)₂. IVB. Plates, m. 162°.⁹⁰

MeEtC(OH)·PO(OH)₂. IVA.^{170, 174} IVB.⁷³ XI.^{170, 174} Crystals, m. 158-9° (from MeOH-Me₂CO).^{170, 174} Benzoate: oil.¹⁷⁰

Diphenyl ester. IVB. Crystals, m. 128.5° (from EtOH).⁷⁶

iso-PrCHOH·PO(OH)₂. IVB. Plates, m. 168-9°.⁹⁰

PrMeC(OH)·PO(OH)₂. IVA.^{171, 174} XI.^{171, 174} Crystals, m. 139-40° (from Me₂CO-Et₂O).^{171, 174}

iso-BuCHOH·PO(OH)₂. IVA.^{169, 174, 223} IVB.^{90, 223} XI.^{169, 174} Crystals, m. 191° (on rapid heating), dec. 183-4° (on slow heating),^{169, 174} m. 188° (from EtOH-EtOAc),²²³ m. 184-5°.⁹⁰

Et₂C(OH)·PO(OH)₂. IVA.^{172, 174} XI.¹⁷² Crystals, m. 108° (from Me₂CO-CHCl₃).¹⁷²

(Me₃C)MeC(OH)·PO(OH)₂. IVB. Oil; isolated as the lead salt.⁷³

EtPrC(OH)·PO(OH)₂. IVB. Oil; isolated as the lead salt.⁷³

n-C₆H₁₃CHOH·PO(OH)₂. IVB.^{73, 90} Crystals, m. 185°, ⁹⁰ m. 165-73° (from water).⁷³

Calcium salt is more soluble in cold water than in hot water.⁹⁰

PhCH(OH)·PO(OH)₂ IVA.^{168, 174} IVB.^{72, 73, 90, 223} XI.^{168, 174} Crystals, m. 195° (from benzene-AcOH),¹⁷⁴ dec. 173° (on slow heating),¹⁷⁴ m. 211°(?),²²³ m. 170-2°.⁷² Aniline salt, m. 201° (from Et₂O).^{72, 73} The most recent preparation of this acid by IVB gives the m. as 177-8°.¹¹¹ Benzoate, m. 93° (from water).¹⁶⁸

Monomethyl ester. IVB. Oil.⁷⁶

Dimethyl ester. XXI.¹⁶⁸ By reduction of the keto analog with sodium amalgam.¹¹¹ Needles, m. 101-2° (from benzene-ligroin),¹¹¹ m. 99°.¹⁶⁸

Monoethyl ester. IVB. Oil.⁷⁶

Diethyl ester. By reduction of the keto analog with sodium amalgam. Prisms, m. 83-4° (from benzene-ligroin).¹¹¹

Monophenyl ester. IVB. Oil.⁷⁶

Diphenyl ester. IVB. Crystals, m. 146° (from MeOH).⁷⁶

PhMeC(OH)·PO(OH)₂. IVA.¹⁷² IVB.⁷⁰ By evaporation of a water solution of the chloro analog at room temperature.⁷⁰ Purest product obtained by XI.¹⁷² Needles, m. 170°.¹⁷² m. 154-5° (from CHCl₃-Et₂O).⁷⁰ Evaporation with hydrobromic acid yields, apparently, the bromo analog, m. 190°.¹⁷²

Diphenyl ester. IVB. Crystals, m. 143.5° (from EtOH).⁷⁶

Ph₂C(OH)·PO(OH)₂. IVA.^{171, 174} IVB.⁷³ XI.^{171, 174} Crystals, m. 184-5° (from water).^{171, 174} m. 171-2°.⁷³

(PhCH₂CH₂)₂C(OH)·PO(OH)₂. IVB. Crystals, m. 173-4° (from benzene).⁷³

(PhCH₂)₂C(OH)·PO(OH)₂. IVB. Crystals, m. 181-2° (from benzene).⁷³

(PhCH₂CH₂)PhC(OH)·PO(OH)₂. IVB. Crystals, m. 165-8° (from benzene).⁷³

HOCH₂·C(OH)Ph·PO(OH)₂. By evaporation of the dichloro or the dibromo analog in water solution on a steam bath. Needles, m. 143-5° (from Me₂CO).⁷⁰

KETO DERIVATIVES

MeCO·PO(OMe)₂. IA.^{111,120} Oil, $b_{6.5}$ 83–5°, ¹²⁰ b_5 76–8°, d_4^{20} 1.2109, n_D^{20} 1.4210.¹¹¹ Cyanohydrin. Oil, $b_{4-4.5}$ 113–3.5°, b_3 95°, d_4^{20} 1.1965, n_D^{20} 1.4092.¹²⁰ *p*-Nitrophenylhydrazone, yellow prisms, m. 189.5–90° (from MeOH).¹¹¹

MeCO·PO(OEt)₂. IA.^{111,120} Oil, b_3 75–80°, ¹¹¹ b_2 70–3°, ¹²⁰ $b_{1.5}$ 60–1°, d_4^{20} 1.0991, n_D^{20} 1.4200.¹¹¹ *p*-Nitrophenylhydrazone, prisms, m. 131–2° (from EtOH).¹¹¹

MeCO·PO(Obu)₂. IA.¹²⁰ Oil, $b_{1.5}$ 87–8°, d_4^{20} 1.0199, n_D^{20} 1.4301.¹²⁰ *p*-Nitrophenylhydrazone, plates, m. 104–4.5° (from Et₂O).¹²⁰ Sodium bisulfite adduct, needles, m. 135–6°. ¹²⁰

MeCO·P(O)OCH(CH₂OMe)CH₂O. IA. Oil, b_2 141–2.5°. ⁸⁵

MeCO·PO(OEt)(OCH₂CHBrCH₂OMe). IA. Oil, b_2 131–2°. ⁸⁵

PhCO·PO(OMe)₂. IA.¹¹¹ Yellow oil, $b_{8.5}$ 144.5–6°, d_4^{20} 1.2400, n_D^{20} 1.5254.¹¹¹ Methanol adduct: cubes, m. 73–6°; ethanol adduct: prisms, m. 63–6°; propanol adduct: m. 84–7°. ¹¹² *p*-Nitrophenylhydrazone, m. 128–9° (from MeOH).¹²⁰ Cyanohydrin. Oil, b_1 143–3.5°, $b_{0.5}$ 131–3°, d_4^{20} 1.2246, n_D^{20} 1.4889.¹²⁰ Sodium bisulfite adduct (dihydrate): needles, m. 84°. ¹²⁰

PhCO·PO(OEt)₂. IA.^{111,142} Yellow oil, $b_{2.5}$ 141°, d_4^{20} 1.1599, n_D^{20} 1.5065.¹¹¹ *p*-Nitrophenylhydrazone, m. 126°, ¹⁴² m. 127–8° (from EtOH).¹¹¹ 2,4-Dinitrophenylhydrazone, m. 171–2°. ¹⁴²

PhCOCH₂PO(OEt)₂. IA. IB. Oil, $b_{2.5}$ 174–6°, d_4^{20} 1.1704.⁸²

MeCOCH₂CH₂PO(OH)₂. Free acid has not been reported.

Di-*n*-decyl ester. IVB–XIV (by heating the intermediate product from MeCOCH:CH₂, phosphorus trichloride, and acetic acid, with decanol).

Oil, $b_{1 \times 10^{-4}}$ 120–70°, d_4^{20} 0.9287, n_D^{20} 1.4528.⁸²

Diphenyl ester. IVB. Oil, $b_{8 \times 10^{-4}}$ 95–112°, d_4^{20} 1.222, n_D^{20} 1.5575.⁸²

PhCO·CCl₂·PO(OH)₂. XVII. Needles, m. 152–3° (from water).⁴³

MeCOCH₂CMe₂·PO(OH)₂. (Diacetonephosphonic acid of Michaelis.) IVB (from mesityl oxide) ^{2, 82} XIII. ^{82, 183} Crystals, m. 63–4° (from water), ⁸ m. 62–3°, ⁸² (said to be the monohydrate; ¹⁸³ anhydrous product, m. 100–10° ¹⁸³). The intermediate, cyclic chloride on reaction with higher alcohols yields a product, m. 143–4° (from dioxane), which has been assigned the cyclic semiesther structure:

Me₂CP(O₂H)OCMe:CH; the possibility of a more complex structure has not been excluded however. ⁸²

Oxime, m. 169–70°. ¹⁸³

Monobutyl ester. XV. Oil, $b_{2 \times 10^{-4}}$ 82–100°, d_4^{20} 1.11, n_D^{20} 1.4590.⁸²

Monodecyl ester. XV. Oil, $b_{1 \times 10^{-4}}$ 104–45°, d_4^{20} 0.98, n_D^{20} 1.4580.⁸²

Diphenyl ester. IVB (from mesityl oxide). Oil, $b_{8 \times 10^{-4}}$ 136–50°, n_D^{20} 1.5531.⁸²

EtBuCH·CH(PO₃H₂)·CH₂COMe. IVB. Crystals, m. 66–9° (from Et₂O).⁸³

(PhCOCH₂)PhCH·PO(OH)₂. IVB. ^{85, 89} Crystals, m. 116° (from Et₂O), ⁸⁵ stated to be the monohydrate, m. 117–8°; ⁸² the anhydrous product, m. 165–7° (from EtOAc).⁸² The intermediate, presumably cyclic, chloride obtained in IVB procedure reacts with alcohols to yield:

Mono-*n*-decyl ester, m. 107–8° (from EtOAc).⁸²

Mono-*n*-dodecyl ester, m. 110–3° (from EtOAc).⁸²

Mono-*n*-tetradecyl ester, m. 112–4° (from EtOAc).⁸²

Mono-*n*-hexadecyl ester, m. 108–10° (from EtOAc).⁸²

Mono-*n*-octadecyl ester, m. 105–9° (from EtOAc).⁸²

Mono-*n*-octadec-9-enyl ester, m. 89–90° (from EtOAc).⁸²

Monophenyl ester. IVB.⁷⁶ By heating the intermediate, cyclic, chloride with phenol.⁶⁹ By treatment of the free acid with thionyl chloride (1 equiv.) and phenol.⁶⁹ Crystals, m. 146°.⁶⁹

Diphenyl ester. IVB.⁷⁶ By heating the acid with thionyl chloride (2 equivs.) and phenol.⁶⁹ Crystals, m. 125°, m. 116–7°.⁷⁶

(PhCO·CHBr)PhCH·PO(OH)₂. By bromination of the above acid in chloroform or by addition of bromine to its intermediate (IVB) reaction mixture.⁶⁹ Crystals, m. 196° (from CHCl₃-ligroin).

Monophenyl ester. By treatment of the above acid with thionyl chloride (1 mole), followed by phenol; better prepared by bromination of the monophenyl ester of the previously listed acid in hot chloroform.⁶⁹ Also obtained by bromination of the presumably cyclic monophenyl ester obtained by heating phenol with the reaction mixture of benzalacetophenone, phosphorus trichloride, and 1 mole of acetic anhydride.⁶⁹ Prepared in small amount by heating the reaction product of bromobenzalacetophenone, acetic acid, and phosphorus trichloride with thionyl chloride, followed by heating with phenol.⁶⁹ Crystals, m. 179°.⁶⁹

(4-MeOC₆H₄)(PhCOCH₂)CH·PO(OH)₂. IVB. Needles, m. 189° (from dil. EtOH).⁶⁶ Oxime, m. 156°.⁶⁵

(4-ClC₆H₄COCH₂)PhCH·PO(OH)₂. IVB.⁷¹ Crystals, m. 112–4° (monohydrate, losing water on melting).⁷¹

Monophenyl ester. By treatment of the acid with thionyl chloride, followed by heating with phenol to 150°, along with the diphenyl ester. By hydrolysis of the diphenyl ester with alcoholic EtONa. Crystals, m. 180° (from CHCl₃).

Diphenyl ester. Prepared as described above. Crystals, m. 109° (from Et₂O).⁷¹

Monomethyl ester. Prepared as described above using MeOH. Crystals, m. 152–3° (from EtOH).⁷¹ May also be obtained by treatment of the dimethyl ester with MeOH-NaOH at room temperature.⁷¹

Dimethyl ester. Prepared as described above. Crystals, m. 123–4°.

(4-ClC₆H₄COCHBr)PhCH·PO(OH)₂. By bromination of the above acid in hot chloroform. Crystals, m. 204°.⁷¹

Monophenyl ester. Two isomers (m. 195–6°, difficultly sol. in 5% sodium bicarbonate, and m. 150–1°, easily sol. in 5% sodium bicarbonate) obtained by bromination of the monophenyl ester of the previously listed acid in CHCl₃ as well as by heating the bromo acid with thionyl chloride, followed by heating with phenol.⁷¹

Diphenyl ester. By bromination of the diphenyl ester of the previously listed acid in CHCl₃. Crystals, m. 127–9°.

Monomethyl ester. By bromination of the monomethyl ester of the previously listed acid in hot CHCl₃, followed by treatment with sodium bicarbonate to destroy the accompanying free bromo acid, which is unstable in alkaline solutions. Crystals, m. 163–4° (from EtOH).⁷¹ If the alkaline treatment (above) utilizes sodium hydroxide, the product is a solid, m. 145–8°, which has 5.1% phosphorus and 10.2% chlorine; it has not been identified.⁷¹

(PhCO)(PhCOCH₂)CH·PO(OH)₂. IVB. Crystals, dec. 183–5° (from EtOAc).

The reaction of the intermediate phosphonyl chloride (presumably cyclic) with the higher alcohols yields a monobasic acid, which has been assigned the cyclic

$$\begin{array}{c} \text{PhCO} \cdot \text{CH} \cdot \text{CH} \cdot \text{CH} \cdot \text{CPh} \cdot \text{O} \cdot \text{P}(\text{O})\text{OH} \\ \text{structure} \end{array}$$

(PhCH·CH·CO·CH₂)PhCH·PO(OH)₂. IVB. Crystals, m. 108° (from dil. EtOH), containing 1.25 molecules of water.⁶⁵

(PhCHBr·CHBr·CO·CH₂)PhCH·PO(OH)₂. By bromination of the above acid in the presence of light. Needles, m. 180–2° (from dil. EtOH), containing 2.5 molecules of water.⁸⁸

(PhCH:CBBr·CO·CH₂)PhCH·PO(OH)₂. By treatment of the above acid with alcoholic potassium hydroxide. Needles, m. 130–2°.⁸⁸

(Ph·CO·CH₂)(Ph·CH:CH)CH·PO(OH)₂. IVB. Crystals, m. 159–61°.⁸⁸

9-Keto-10-hydroxyphenanthrene-10-phosphonic acid. IVB. Reddish crystals, m. 125–8° (from dil. HCl). Yields green solutions in potassium hydroxide.⁹⁰

3-Phosphonomethylene camphor. Apparently a form of IC reaction, in which 3-hydroxymethylenecamphor is treated with somewhat less than an equimolar amount of phosphorus trichloride, followed by hydrolysis. Needles, m. 113–5° (from water).¹⁹¹ Originally believed to be an ester of phosphorous acid.⁵⁰ Aniline salt, m. 195–6°.

Diethyl ester. XV. Oil, b₂₀ 195–205°.¹⁹¹

CARBOXYLIC DERIVATIVES

HO₂C·PO(OH)₂. The acid is too unstable to be isolated.

Triethyl ester. IA.^{17, 18, 220} IB.^{23, 220, 221, 222} Liquid, b_{12.5} 138.25°,¹⁷ b_{12.5} 132.25°,¹⁸ b₁₂ 135.3°,¹⁸ b₁₀ 130–1°,²³ b_{8–10} 122.5–3.0°,^{220, 222} d₄⁰ 1.1422.¹⁷

(C)-Ethyl (P)-ethyl (P)-3-methoxy-2-chloropropyl ester. IA.³⁵ Liquid, b_{1.5} 144.5–46°, n_D²⁰ 1.4520.³⁵

(C)-Amide (P)-diethyl ester. From the triethyl ester (above) and ammonium hydroxide at room temperature. Needles, m. 134–5° (from benzene).^{220, 222}

HO₂CCH₂PO(OH)₂. XIV.^{18, 21, 123, 220, 222} Crystals, m. 142–3°,^{221, 222} m. 139.5° (from AcOH).¹⁸ Tribasic to thymolphthalein.^{221, 222}

(C)-Ethyl ester. By warming the acid with ethanolic HCl. Oil.²²⁰

(C)-Methyl (P)-diethyl ester. IB. Liquid, b₉ 131.5–2°.²²⁰

Triethyl ester. IA.^{5, 17, 220} IB.^{17, 18, 21, 140, 220, 222} Liquid, b₂₀ 152–3°,²¹ b_{14–15} 147–9°,^{21, 222} b₁₂ 149–50°,¹⁷ b₁₀ 140–3°,¹³⁷ b₁₀ 138.5°,¹⁸ b_{8–10} 140°,²²² b_{9–10} 140–1°,²¹ d₄⁰ 1.1392.¹⁷ On treatment with sodium or potassium the ester readily forms the corresponding metallic derivatives, analogous to the malonate derivatives.²¹ On being heated with dilute acids or alkalis the triethyl ester yields what appears to be a (P)-monoethyl ester, a sirup, that forms a disilver salt (needles, from water).²²⁰

(C)-Ethyl (P)-diisobutyl ester. IB.^{22, 123} Liquid, b₁₀ 170–1°, d₄⁰ 1.0363, d₁₆¹⁷ 1.0212.^{22, 123}

Tri-*n*-butyl ester. IB. Oil, b₉ 152–6°, n_D²⁵ 1.4365.¹⁴⁰

(C)-Phenyl (P)-diethyl ester. IA.²² IB.²² Oil, b₉ 153.5–7°.²²

(C)-Amide (P)-diethyl ester. From the triethyl ester and ammonium hydroxide at room temperature. Needles, m. 78–80° (from benzene).²²⁰

(C)-Diphenylamide (P)-diethyl ester. IA. Crystals, m. 67–8° (from ligroin).²²⁵ The sodio derivative forms crystals, m. 162–4°.²³⁵

(C)-Isopropylidenehydrazide. By heating the triethyl ester with hydrazine, followed by the treatment of the resulting crude product with acetone. Needles, m. 185–6° (from EtOH).²²⁰

HO₂C·CHMe·PO(OH)₂. XIV. Crystals, m. 119–32°.^{18, 21}

Triethyl ester. IA.¹⁷ By treatment of the sodium or the potassium (better) derivative of triethyl phosphonoacetate with methyl iodide.^{18, 21} Liquid, b₁₂ 143–4°,¹⁸ b₁₀ 138.5–8.75°,¹⁷ b₈ 126.5–7°,²¹ d₄⁰ 1.111.¹⁷

(C)-Phenyl (P)-diethyl ester. From the metallic derivative (see above) of

the corresponding phosphonoacetate, by treatment with methyl iodide.
Oil, $b_{7.5}$ 165–8.5°. ³²

HO₂CCMeOH·PO(OH)₂. IVB (from pyruvic acid). Very hygroscopic solid, m. 165–70° (from AcOH). Aniline salt, m. 213°; *p*-toluidine salt, m. 211°; phenylhydrazine salt, m. 184°. ⁴⁸ Tribasic to thymolphthalein. ⁴⁸

HO₂C·CH₂·CH₂PO(OH)₂. XIV. ^{18, 26, 221, 222} Plates, m. 167–8°, ¹⁸ m. 170°, ²⁵ m. 178–80°. ^{221, 222} Tribasic to thymolphthalein. ^{221, 222}

(C)-Ethyl ester. By warming the acid with ethanolic HCl. Plates, m. 64.5–66° (from benzene). ^{221, 222}

Triethyl ester. IA. ^{17, 26, 222} IB. ^{26, 87, 221} Liquid, b. 287–8°, ²⁶ b_{12} 171–2°, ¹⁸ b_{12} 167°, ¹⁷ b_{10} 167–8°, ¹⁸ b_{10} 151°, ²⁶ b_{10} 149.5–50°, ²²¹ b_8 140–2°, ²²¹ d_0^0 1.1162, ²⁶ d_0^0 1.1177, ¹⁷ $d_0^{16.7}$ 1.1021, ²²¹ d_0^{17} 1.1015. ²⁶ It is best made by the IB procedure using potassium diethyl phosphite. ²⁶

(C)-Amide (P)-diethyl ester. From the triethyl ester (above) and ammonium hydroxide at room temperature. Needles, m. 61–2.5° (from benzene). ^{221, 222}

(P)-Monoethyl ester. XIV (from triethyl ester). Oil, which forms a crystalline disilver salt. ²²¹

HO₂C·CHEt·PO(OH)₂. Free acid has not been reported.

Triethyl ester. IA. ¹⁷ Oil, $b_{10.5}$ 147.5–8°, d_0^0 1.0919. ¹⁷

HO₂C·CH₂·CH₂·CH₂PO(OH)₂. XIV (from the cyanopropyl derivative). Prisms, m. 127–8.5° (from water). ^{221, 222}

(C)-Ethyl ester. By warming the acid with ethanolic HCl. Prisms, m. 76–7° (from benzene). ^{221, 222}

HO₂C·CMe₂·PO(OH)₂. By oxidation of MeCO·CH₂·CMe₂·PO(OH)₂ with fuming nitric acid. Colorless crystals; yields a crystalline trisilver salt. ^{3, 153}

***n*-C₆H₁₃CH(CO₂H)PO(OH)₂.** XIV. Liquid. Forms a sparingly soluble acid sodium salt. ⁵⁷

Triethyl ester. From sodium derivative of EtO₂CCH₂PO(OEt)₂ and hexyl bromide. Liquid, $b_{1.5-2}$ 155–7°. ⁵⁷

HO₂C(CH₂)₁₀PO(OH)₂. XIV. Crystals, m. 110–1°. ⁵⁸

(C)-Ethyl (P)-dibutyl ester. IB. Liquid. ⁵⁸

HO₂C·CH(CH₂Ph)·PO(OH)₂. XIV. Hygroscopic solid, m. 137–45°. ³¹

Triethyl ester. From the potassium derivative of triethyl phosphonoacetate and benzyl chloride, in very poor yield. The sodium derivative yields too small an amount to be isolated. Liquid, b_3 180–80.5°, d_0^0 1.1349. ³¹

(HO₂C·CO·CH₂)PhCH·PO(OH)₂. By ozonization of PhCH(PO₃H₂)CH₂CO·-CBr:CHPh. Crystals, dec. 183°. ⁶⁸

(HO₂C)₂CH·PO(OH)₂. Free acid is too unstable for isolation.

(C)-Diethyl (P)-dimethyl ester. IA. Liquid, b_{3-4} 153–4°, d_0^0 1.2332, d_0^{16} 1.2184, n_D^{14} 1.4525. ²³

Tetraethyl ester. IA. ^{23, 140} Yellow liquid, b_{3-4} 154–6°, ²³ b_2 153–6°, ¹⁴⁰ d_0^0 1.1719, d_0^{16} 1.1559, ²³ n_D^{19} 1.4450, ²³ n_D^{25} 1.4358. ¹⁴⁰

(C)-Diethyl (P)-dipropyl ester. IA. Liquid, b_{3-4} 169–70°, d_0^0 1.1236, d_0^{14} 1.1117, n_D^{18} 1.4430. ²³

¹ (C)-Diethyl (P)-dibutyl ester. IA. ^{23, 140} IB. ¹⁴⁰ Yellow oil, b_{3-4} 185–90° (with decomposition), n_D^{16} 1.4405. ²³

DIPHOSPHONIC ACID DERIVATIVES

(HO)₂P(O)CH₂PO(OH)₂. XIV. Crystals, m. 200–1° (from AcOH). ²²²

(P,P')-Diethyl ester. Disodium salt obtained by IB. ²²² Crystals (from EtOH)

Disilver salt, needles (from dil. EtOH). ²²²

162 ACID DERIVATIVES WITH CARBON TO PHOSPHORUS LINK

- Tetraethyl ester. IA.⁸⁶ Oil, $b_{1.5}$ 143°, $n_D^{16.5}$ 1.4312.⁸⁸
- (HO)₂P(O)CH₂CH₂PO(OH)₂. XIV. Plates, m. 220–1° (from AcOH).¹¹⁷
- Tetraethyl ester. IA.^{86, 239} IB.²³⁹ Liquid, b_{15} 203–6°, ²³⁹ b_{14} 200–2°, ²³⁹ $b_{2.5}$ 180°, ⁸⁸ b_1 167°, ⁸⁸ $n_D^{16.5}$ 1.4425.⁸⁸
- Tetraphenyl ester. IA. Needles, m. 155–5.5° (from MePh).¹¹⁷
- Di-*o*-phenylene ester. IA. Glass, m. about 196°, b_5 265°.¹¹⁷
- (HO)₂P(O)(CH₂)₃PO(OH)₂. XIV. Crystals, m. 168–9°, ¹³⁶ m. 170.5–2.0° (from water).^{221, 222}
- Tetraethyl ester. IA.^{88, 136} IB.^{221, 222} Liquid, b_8 198–9°, ^{221, 222} b_2 170–2°, ¹³⁶ $b_{0.8}$ 175°, ⁸⁸ $d_4^{18.6}$ 1.1278, ^{221, 222} $n_D^{16.5}$ 1.4508.⁸⁸
- (HO)₂P(O)CH₂OCH₂PO(OH)₂. XIV. Needles, m. 96–8° (from water).¹
- (P,P')-Diethyl ester. Disodium salt obtained by heating the tetraethyl ester with sodium chloride or bromide. Glassy solid, m. 51–8°; the similar dipotassium salt, m. 52–4°.^{1, 2}
- Tetraethyl ester. IA.¹ IB.^{1, 2} Liquid, $b_{7.5}$ 193–4°, b_6 192.5–3.5°, d_{16}^{15} 1.188, n_D^{15} 1.4467, n_D^{20} 1.4470.^{1, 2}
- p*-(HO)₂P(O)CH₂·C₆H₄CH₂PO(OH)₂. XIV. Solid, m. 268–71°.¹⁵⁶
- Tetraethyl ester. IA. Solid, m. 72–3°, b_2 204°.¹⁵⁶
- 2,4-Me₂C₆H₃(1,5)(CH₂PO₃H₂)₂. XIV. Solid, m. 264°.¹⁵⁶
- Tetraethyl ester. IA. Liquid, b_2 192–4°, d_{20}^{20} 1.1383, n_D^{20} 1.4985.¹⁵⁶
- 2,5-Me₂C₆H₃(1,4)(CH₂PO₃H₂)₂. XIV. Solid, m. 340–50°.¹⁵⁶
- Tetraethyl ester. IA. Solid, m. 58–9°.¹⁵⁶
- 1,4-(HO)₂P(O)CH:CPh·C₆H₄·CPh:CHPO(OH)₂. II. Crystals, m. 210°.⁴⁵
- 1,3,5-Me₃C₆H(2,4)(CH₂PO₃H₂)₂. XIV. Powder, does not melt at 300°.¹³⁹
- Tetrabutyl ester. IB. Crystalline mass.¹³⁹
- 9,10-Di-(phosphonomethyl)-anthracene. XIV. Needles, dec. 215°.¹³⁹
- Tetrabutyl ester. IB. Solid (obtained in crude state).¹³⁹

DERIVATIVES WITH PHOSPHORUS BONDED TO AN AROMATIC RING

- PhPO(OH)₂. X.^{153, 178, 196} XI.¹⁷⁹ XIII.^{177, 179, 196, 200, 219, 252} XIV.¹⁴⁹ XVI.^{182, 161} Plates, m. 161–2°, ²⁵² m. 158–60°, ²¹⁹ m. 158–9°, ¹⁴⁹ m. 158°, ^{177, 179} m. 156°.¹⁶¹ Best crystallized from water.¹⁴⁹
- Dimethyl ester. XXI. Liquid, b 247°.^{179, 190}
- Monoethyl ester. XV. Unstable oil, yielding a crystalline silver salt.¹⁷⁹
- Diethyl ester. III.¹⁴⁹ X.⁹⁴ XXI.^{179, 190} Liquid, b 267°.^{179, 190} b_2 121–3°, $b_{1.5}$ 117–8°, ¹⁴⁹ $b_{0.5}$ 104–5°, ¹⁴⁶ n_D^{25} 1.4935.¹⁴⁹
- 1,2-Ethylene ester (cyclic). XV. Liquid, b_{6-7} 210°.²⁴⁷
- 1,3-Propylene ester (cyclic). XV. Liquid, $b_{7.5}$ 212–4°.²⁴⁷
- Diallyl ester. XV. Liquid, b_1 128°, ²⁵² b_1 126–8°, ²⁴⁹ d_4^{25} 1.1097, ²⁵² d^{25} 1.112, ²⁴⁹ n_D^{25} 1.5128, ²⁵² n_D^{25} 1.5106.²⁴⁹
- 2,3-Butylene ester (cyclic). XV. Liquid, b_{15} 210–5°.²⁴⁷
- Dibutyl ester. XV. Liquid, b_4 166°.²⁴⁸
- Dimethallyl ester. XV. Liquid, b_{2-3} 140–3°, d_4^{25} 1.0728, n_D^{25} 1.5057, n_D^{25} 1.5057.^{249, 253}
- Di-*n*-amyl ester. XV. Liquid, b_8 170°.²⁴⁸
- Di-2-ethylhexyl ester. XV. Liquid, b_4 204–7°.²⁴⁸
- Dicyclohexyl ester. XV. Liquid.²⁴⁸
- Di-2-ethoxyethyl ester. XV. Liquid, b_{17} 220°.²⁴⁸
- Di-2-butoxyethyl ester. XV. Liquid, b_4 207–10°.²⁴⁸
- Monophenyl ester. XV. Needles, m. 57°; silver salt: needles (from hot water).^{179, 196}

Diphenyl ester. XV. Needles, m. 73–4°,²¹⁷ m. 63.5°,^{179, 195} b. 370–80°, b₂₀ 260–70°.²¹⁷

Di-*p*-chlorophenyl ester. XV. Crystals, m. 67.5–9.5°, b₁₃ 276–7°.²¹⁷

o-Phenylene ester (cyclic). XV. Crystals, m. 124–5°, b₉ 206°.⁴

Di-*p*-butylphenyl ester. XV. Liquid, b₂₀ 305–18°.²¹⁷

3-O₂NC₆H₄PO(OH)₂. By nitration of the above acid with cold fuming nitric acid.^{146, 219} An older procedure employs 100° heating.¹⁹⁰ Needles, m. 140° (from Et₂O-benzene).^{190, 219} Barium salt is soluble in water.¹⁹⁰

3-H₂NC₆H₄PO(OH)₂. By reduction of the above acid with tin and hydrochloric acid¹⁹⁰ or, better, with ammonium sulfide²¹⁹ or sodium sulfide.¹⁴⁶ Needles, dec. 280°,¹⁹⁰ dec. 290°,¹⁴⁶ dec. 275–80°.²¹⁹ Slightly soluble in water.²¹⁹ The diazonium nitrate forms prisms, m. 188° (from water), which explode above the melting point.¹⁹⁰ Nitration is best performed on the carbethoxy derivative.²¹⁹

3-EtO₂CNH·C₆H₄PO(OH)₂. From the above acid and ethyl chlorocarbonate. Plates, m. 140° (from Me₂CO).²¹⁹ Nitration at 15° with nitric acid in acetic acid or anhydride yields a nitro derivative, m. 165° (with decomposition). On hydrolysis with hydrochloric acid it yields the free acid, m. 185° (from 60% EtOH), which has a nitro group in either 2- or 4- position.²¹⁹

3-H₂N-2,4,6-Br₃C₆H·PO(OH)₂. By treatment of the amino acid with bromine water in the cold. Needles, m. 222° (from water).²¹⁹

4-H₂NC₆H₄PO(OH)₂. By heating the 4-chloro acid with ammonium hydroxide to 150° in the presence of fresh cuprous oxide.^{42, 142} Very low yields result with metallic copper catalyst.^{42, 86} Substitution of the 4-bromo acid permits the reaction to be carried out at 100°.* Colorless powder, very sparingly soluble in water.⁴² On rapid heating, m. 245°, with resolidification and remelting to a blue liquid at 285°.^{42, *} Diethylamine salt, m. 212° (from water); ethanolamine salt, plates, m. 178°.* Reaction with acyl chlorides in sodium bicarbonate solution yields the following N-acyl derivatives: acetyl, m. 229°; butyryl, m. 284°; caproyl, m. 204°; benzoyl, m. 287°; succinyl, m. 276°.^{42, *} N-Carbamido derivative, isolated as the ammonium salt (does not melt at 300°) by heating the free acid with urea to 120°.* Diazotization and coupling with phenols or amines give the following coupling products (azo compounds): with resorcinol, red, m. 211°; with *m*-phenylenediamine, red solid; with pyrrol, violet solid.*

4-H₂N-3-O₂N·C₆H₃PO(OH)₂. By heating the 4-chloro derivative with conc. ammonium hydroxide to 150°. Plates, dec. 231° (from water).²¹⁹

3-ClC₆H₄PO(OH)₂. By diazo reaction from the 3-amino derivative. Needles, m. 136–7° (from 1:1 HCl).¹⁴⁶

3-BrC₆H₄PO(OH)₂. By diazo reaction, as above. Plates, m. 152–3°.¹⁴⁶

3-IC₆H₄PO(OH)₂. By diazo reaction, as above. Plates, m. 182–3°.¹⁴⁶

4-ClC₆H₄PO(OH)₂. XIII.^{42, 184, 219} XIV.¹⁴⁹ Needles (from water) or plates (from EtOH), m. 188° (from EtOAc),⁴² m. 187–8°,¹⁴⁹ m. 184–5°,¹⁸⁴ m. 184°.²¹⁹ Acid ammonium salt is sparingly soluble in water; soluble in hot alcohol.⁴²

Diethyl ester. III.¹⁴⁹ Liquid, b₄ 144–6°, b_{1.5} 117–9°, n_D²⁵ 1.5068.¹⁴⁹

Diallyl ester. XV. Liquid, b₂ 136–9°, n_D²⁵ 1.5208.²⁶²

Dimethallyl ester. XV. Liquid, b₁ 137–40°, n_D²⁵ 1.5162°.²⁶²

4-Cl-3-O₂NC₆H₃PO(OH)₂. By nitration of the 4-chloro acid with fuming nitric acid,¹⁸⁴ or by similar treatment of the corresponding chlorophosphonous acid.^{30, 219} Needles, m. 166–8°,¹⁸⁴ m. 166°.^{30, 219}

* Limaye, Bhide, personal communication.

4-Cl-3-H₂NC₆H₃PO(OH)₂. By reduction of the above acid with tin and hydrochloric acid. Needles, dec. 270° (from water).¹⁸⁴ Heating the aqueous solution of monosodium salt of the 3-nitro-4-chlorobenzenephosphonic acid with an excess of the amines at 120° results in the following derivatives:³⁹

4-PrNH-3-O₂NC₆H₃PO(OH)₂, yellow needles, dec. 178-9°.

4-BuNH-3-O₂NC₆H₃PO(OH)₂, yellow needles, dec. 176-8°.

4-iso-BuNH-3-O₂NC₆H₃PO(OH)₂, yellow rods, dec. 176-80°.

4-AmNH-3-O₂NC₆H₃PO(OH)₂, yellow rods, m. 132-4°.

4-iso-AmNH-3-O₂NC₆H₃PO(OH)₂, needles, dec. 171-3°.

4-(HOCH₂CH₂NH)-3-O₂NC₆H₃PO(OH)₂, orange plates, dec. 182°.

4-(O(CH₂CH₂)₂N)-3-O₂NC₆H₃PO(OH)₂, orange prisms, m. 176°.

Hydrogenation of these in the form of monosodium salts in water in the presence of Raney nickel yields the amino analogs:

4-PrNH-3-H₂NC₆H₃PO(OH)₂, needles, m. above 200°.

4-BuNH-3-H₂NC₆H₃PO(OH)₂, needles, m. above 200°.

4-iso-BuNH-3-H₂NC₆H₃PO(OH)₂, needles, m. above 200°.

4-AmNH-3-H₂NC₆H₃PO(OH)₂, needles, m. above 200°.

4-iso-AmNH-3-H₂NC₆H₃PO(OH)₂, needles, m. above 200°.

4-(HOCH₂CH₂NH)-3-H₂NC₆H₃PO(OH)₂, needles, m. above 200°.

4-(O(CH₂CH₂)₂N)-3-H₂NC₆H₃PO(OH)₂, brown powder, m. above 200°.

4-(HO₂CCH₂NH)-3-O₂NC₆H₃PO(OH)₂. By heating the 4-chloro acid (above) with glycine in isoamyl alcohol with sodium carbonate to 145°. Yellow rods, m. above 200°.³⁹ Hydrogenation (as described above) yields a dehydration product: 1,2,3,4-tetrahydro-3-oxo-6-quinoxalinephosphonic acid, needles, m. above 200°.³⁹

4-PhO-3-O₂NC₆H₃PO(OH)₂. By heating the 4-chloro analog with phenol and potassium carbonate with copper bronze to 125°. Tan needles, m. over 200°.³⁹ Reduction (as described above) yields 4-PhO-3-H₂N-C₆H₃PO(OH)₂, gray needles, m. above 200°.³⁹

4-(2-ClC₆H₄O)-3-O₂NC₆H₃PO(OH)₂. By heating the 4-chloro analog with chlorophenol (as above) in isoamyl alcohol at 145°. Tan crystals, m. above 200° (from dil. AcOH).³⁹ Reduction (as described above) yields 4-(2-ClC₆H₄O)-3-H₂NC₆H₃PO(OH)₂, needles, m. over 200°.³⁹

4-(4-ClC₆H₄O)-3-O₂NC₆H₃PO(OH)₂. As above, using *p*-chlorophenol. Tan crystals, m. over 200° (from dil. AcOH).³⁹ Reduction (as above) yields 4-(4-ClC₆H₄O)-3-H₂N-C₆H₃PO(OH)₂, gray needles, m. above 200°.³⁹

4-HO-3-O₂NC₆H₃PO(OH)₂. By refluxing the corresponding 4-chloro acid with 4 *N* sodium hydroxide. Yellow crystals, m. 214-6° (from water).³⁹ Reduction (as described above) yields 4-HO-3-H₂N-C₆H₃PO(OH)₂, brown needles, m. above 200°.³⁹

4-Me₂NC₆H₄PO(OH)₂. XI (best with mercuric chloride). Crystals, m. 133° (from EtOH); not very stable in water solution.^{207, 208}

3,4(?) -Cl₂C₆H₃PO(OH)₂. XIV. Crystals, m. 153°; acid sodium salt, m. 260° (with decomposition).¹⁴⁹

Diethyl ester. III. Liquid, *b*₂ 155-7°, *b*_{1.5} 142-3°, *n*_D²⁵ 1.5191.¹⁴⁹

2,5-Cl₂C₆H₃PO(OH)₂. XIV. Crystals, m. 194-7° (from dil. EtOH; monohydrate).¹⁴⁹

Diethyl ester. III. Liquid, *b*₃ 160-4°, *n*_D²⁵ 1.5105.¹⁴⁹

4-BrC₆H₄PO(OH)₂. XIII.¹⁸⁴ XIV.¹⁴⁶ Needles, m. 202°,¹⁸⁴ m. 198-9°.¹⁴⁶ The residues from the isolation of the intermediate dichlorophosphine yield, after the usual treatment, an apparent isomer, m. 265°.¹⁸⁴

Diethyl ester. III. Liquid, *b*_{0.5} 126-8°, *n*_D²⁵ 1.5188.¹⁴⁶

- 4-Br-3-O₂NC₆H₃PO(OH)₂.** By nitration of the above acid with fuming nitric acid at 100°. Crystals, m. 185°. ¹⁸⁴
- 4-IC₆H₄PO(OH)₂.** By diazo reaction from the 4-amino acid. Plates, m. 228-9° (from HCl). ¹⁴⁶
- 4-MeOC₆H₄PO(OH)₂.** XIII. Rhombic crystals, m. 158° (from water). ¹⁸⁴
- 4-MeO-3(?) -O₂NC₆H₃PO(OH)₂.** By nitration of the above acid with fuming nitric acid. Needles, m. 187° (from EtOH). ¹⁸⁴
- 4-EtOC₆H₄PO(OH)₂.** XIII. Needles, m. 165° (from water). ¹⁸⁴
- 4-PhOC₆H₄PO(OH)₂.** XIII. Plates (monohydrate), m. 185° (from AcOH). On heating to 180° this monohydrate loses 1.5 molecules of water and yields a glass. ⁷⁹
- 4-BrC₆H₄OC₆H₄PO(OH)₂.** By bromination of the above acid in hot CHCl₃. Crystals, m. 209° (from AcOH). ⁷⁹
- 2-MeC₆H₄PO(OH)₂.** XIII. ²⁰⁴ XI. ¹⁸⁴ Crystals, m. 141° (from EtOH-benzene), readily soluble in water. ^{184, 204} Chlorination of a concentrated aqueous solution yields *o*-chlorotoluene. ^{184, 204}
- 2-Me-5(?) -O₂NC₆H₃PO(OH)₂.** By nitration of the above acid with warm fuming nitric acid. Needles, m. 174° (from water). ¹⁸⁴
- 2-Me-5(?) -H₂NC₆H₃PO(OH)₂.** By reduction of the above acid with tin and hydrochloric acid. Brown needles, m. 280-300° (with decomposition). Slightly soluble in water. ¹⁸⁴
- 2-Me-5-ClC₆H₃PO(OH)₂.** By chlorination of the 2-methyl derivative in very dilute, ice-cooled aqueous solution. Crystals, m. 205° (from dil. EtOH). Some dichloro acid (possibly 3,5-), m. 240°, is formed as a by-product. ¹⁸⁴
- 2-HO₂CC₆H₄PO(OH)₂.** By oxidation of the 2-methyl derivative with dilute permanganate at 50°. Needles, m. 172° (from water). On heating with an excess of phosphorus pentachloride, it yields 2-Cl(O)CC₆H₄POCl₂, m. 54°. ¹⁸⁴
- 3-MeC₆H₄PO(OH)₂.** XIII. Needles, m. 116-7° (from water). The neutral barium salt is soluble in water. ¹⁸⁴
- 3-Me-6-ClC₆H₃PO(OH)₂.** By careful chlorination of the above acid in aqueous solution at room temperature. Needles, m. 176° (from water). ¹⁸⁴
- 3-Me-2,5,6-Cl₃-C₆H-PO(OH)₂.** By prolonged chlorination of 3-methyl derivative in water. Needles, m. 220° (from water). ¹⁸⁴
- 3-Me-6-BrC₆H₃PO(OH)₂.** By careful bromination of the 3-methyl acid in warm aqueous solution. Needles, m. 198° (from water). ¹⁸⁴
- 3-HO₂CC₆H₄PO(OH)₂.** By oxidation of the 3-methyl derivative with permanganate at 50°. ¹⁸⁴ Needles, m. 245-6° (from EtOH). ¹⁸⁴ Warming with an excess of phosphorus pentachloride yields 3-Cl(O)CC₆H₄POCl₂, m. 61°. ¹⁸⁴
- 4-MeC₆H₄PO(OH)₂.** XIII. ^{182, 181, 184, 202, 204} XIV. ¹⁴⁹ Needles, m. 189° (from water), ²⁰² m. 187.5-9°. ¹⁴⁹ The sparingly soluble acid potassium salt is characteristic of many phosphonic acids and phosphates. Its dimer character was suggested by Michaelis many years before similar studies on phosphate esters were made (see Phosphates).
- Diethyl ester. III. Liquid, b₁ 122° (fractionated from the isomer mixture, which b₁ 108-22°), n_D²⁵ 1.4912. ¹⁴⁹
- Diallyl ester. XV. Liquid, b₃ 127-8°, ²⁴⁹ b₁ 134-6°, ²⁵² d₄²⁵ 1.089, n_D²⁵ 1.5120, ²⁵² n_D²⁸ 1.5097. ²⁴⁹
- Dimethallyl ester. XV. Liquid, b₃₋₄ 137-9°, ²⁴⁹ b₁ 146-9°, ²⁵² d₄²⁵ 1.057, n_D²⁵ 1.5070, ²⁵² n_D²⁸ 1.5065. ²⁴⁹
- Diphenyl ester. XV. Liquid, b. over 360°. ¹⁸⁴
- Di-*p*-tolyl ester. XV. Liquid, b. over 360°. ¹⁸⁴
- o*-Phenylene ester (cyclic). XV. Crystals, m. 81°. ¹⁸⁴

- 4-Me-3-O₂NC₆H₃PO(OH)₂.** By nitration of the above acid with fuming nitric acid at 100° and purified through the barium salt. Yellow needles, m. 191° (from water).¹⁸⁴
- 4-Me-3-H₂NC₆H₃PO(OH)₂.** By reduction of the above acid with tin and hydrochloric acid. Needles, m. 290° (with decomposition).¹⁸⁴
- Diethyl ester. XXI. Undistillable,¹⁸⁴ as is the corresponding ester of the nitro derivative (above).
- 4-Me-3-ClC₆H₃PO(OH)₂.** XIII. Plates, m. 190° (from water). Aniline salt, m. 216°. Heated with fuming nitric acid, this acid forms a nitro derivative, m. 200° (from water).¹⁷⁶
- 4-Me-3,5(?)-(O₂N)₂C₆H₂PO(OH)₂.** By prolonged nitration of the 4-methyl derivative with fuming nitric acid at 100°. Yellow plates, m. 251° (from ether).¹⁸⁴
- 4-HO₂CC₆H₄PO(OH)₂.** By oxidation of the 4-methyl or the 4-ethyl derivative with permanganate at 50°. Plates or needles, m. over 300°. Acid potassium and sodium salts are sparingly soluble in water; trisilver salt forms water-soluble needles. Heating with an excess of phosphorus pentachloride forms the trichloride, m. 83°, b. 315°, which on treatment with dry ammonia (which probably forms the triamide), followed by boiling with water (for hydrolysis of P-amide groups), yields the (C)-amide, needles, m. over 300°. ¹⁸⁴
- (C)-Monoethyl ester. By passage of hydrogen chloride into an alcoholic solution of the acid. Needles, m. 78°. ¹⁸⁴
- Trimethyl ester. XXI. Undistillable oil.¹⁸⁴
- 4-HO₂C-3-Cl-C₆H₃PO(OH)₂.** By oxidation of the corresponding 4-methyl derivative with permanganate at 50°. Plates, m. 254°. ¹⁷⁶
- 4-EtC₆H₄PO(OH)₂.** XIII. Needles, m. 164° (from water).¹⁸⁴
- 2,4-Me₂C₆H₃PO(OH)₂.** XIII. Needles, m. 194°; soluble 1.5% in water at 20°; 6.9% at 100°. ²⁶¹ Nitration with fuming nitric acid forms two nitro derivatives, which m. 182° and m. 100°. ²⁶¹ Oxidation of the acid with permanganate at 50° yields a monocarboxylic acid: prisms, m. 262° (from water); this, on heating with an excess of phosphorus pentachloride, yields the corresponding acid chloride, b. 310°. ²⁶¹
- 3,5-Me₂C₆H₃PO(OH)₂.** XIII. It was separated at this stage of synthesis from the 2,4-isomer, formed simultaneously in the preparation of the dichlorophosphine by the Friedel-Crafts reaction. Plates or needles, m. 161°; soluble 1.8% in water at 15°; 117% at 100°. ²⁶¹ Fuming nitric acid yields a nitro derivative, m. 107°, while oxidation with permanganate at 50° yields a monocarboxylic derivative, m. 220°, which forms the corresponding acid chloride, b₁₄₇ 249°, on heating with an excess of phosphorus pentachloride. ²⁶¹
- 2,5-Me₂C₆H₃PO(OH)₂.** XIII. Needles, m. 179–80° (from water). Treatment with fuming nitric acid yields a nitro derivative, m. 224°, while oxidation of permanganate yields a monocarboxylic derivative, m. 278° (from dil. EtOH), which on treatment with an excess of phosphorus pentachloride yields the corresponding acid chloride, m. 62°. ²⁶¹
- 4-(?)-iso-PrC₆H₄PO(OH)₂.** XIII. Needles, m. 139° (from CS₂). Phenylhydrazine salt, m. 172°; aminoazobenzene salt, m. 185°. ¹⁸⁴ Mild oxidation with dilute permanganate yields an oily hydroxy acid, which is apparently of type Me₂C(OH), as on heating to 120° it yields an unsaturated acid, probably 4-CH₂:CMe·C₆H₄-PO(OH)₂, a yellow powder. ¹⁸⁴
- 2,4,5-Me₃C₆H₂PO(OH)₂.** XIII. Plates or needles, m. 212° (from water); soluble 0.82% in water at 19°; 2.55% at 100°. ¹⁸⁴ Although bromine water yields bromotrimethylbenzene, with elimination of phosphorus, chlorine water in addition to

such elimination reaction yields a small amount of a chloro derivative (see below).¹⁸⁴ Fuming nitric acid in the cold yields a dinitro derivative (obviously only 3,6- is possible) needles, m. 239° (from water), which forms a phenylhydrazine salt, dec. 240°.¹⁸⁴

Diphenyl ester. XV. Crystals, m. 62.5°, b. over 360°.¹⁸⁴

2,4,5-Me₃-6-ClC₆H-PO(OH)₂. By chlorination of the above acid, best in acetic acid solution, until chloropseudocumene formation becomes evident (cloudy test with alkali). Needles, m. 235° (from AcOH). Phenylhydrazine salt, m. 197.5° (from EtOH).¹⁸⁴ Fuming nitric acid in the cold yields the 3-nitro derivative (best purified through the insoluble lead salt), m. 227-8° (from water).¹⁸⁴

2,4-Me₂-5-(HO₂C)C₆H₂PO(OH)₂. By oxidation of the trimethyl derivative with 2 molecules of permanganate at 60-70°. Powder, m. 258° (from water).¹⁸⁴

4-Me-2,5-(HO₂C)₂C₆H₂PO(OH)₂. By oxidation of the trimethyl derivative with 4 molecules of permanganate. Hygroscopic powder, m. 185-90°. The location of the carboxyls is given only provisionally.¹⁸⁴

2,4,6-Me₃C₆H₂PO(OH)₂. XIII. Needles, m. 167° (from dil. EtOH). Oxidation with 2 molecules of permanganate yields a monocarboxylic derivative (probably 2-), m. 245°, whereas the use of 4 molecules of the oxidant yields a dicarboxylic derivative (possibly 2,6-), m. 255°.¹⁸⁴

2(or 5)-Me-5(or 2)-iso-PrC₆H₃PO(OH)₂. XIII. Oily liquid. Phenylhydrazine salt, m. 156°.¹⁸⁴

1-C₁₀H₇PO(OH)₂. XIII.^{128, 152} Needles, m. 190°, ¹²⁸ m. 189° (from hot water).¹⁸²

PhC₆H₄PO(OH)₂. XIII. Obtained only as an isomer mixture.^{183, 184, 185}

4(?) -PhCH₂C₆H₄PO(OH)₂. XIII. Needles, m. 196° (from dil. EtOH). Phenylhydrazine salt, m. 187°.¹⁸⁵

4(?) -Ph-CO-C₆H₄PO(OH)₂. By oxidation of the above acid with permanganate at 50°. Plates, m. 204° (from EtOH). Phenylhydrazine salt, m. 124°. Heating the acid with an excess of phosphorus pentachloride yields PhCCl₂C₆H₄POCl₂, a crystalline solid, m. 64°, b₁₆ 258°.¹⁸⁵

Diethyl ester. XXI. Undistillable oil, which forms a solid oxime.¹⁸⁸

4-PhCH₂CH₂C₆H₄PO(OH)₂. XI. XIII. Plates, m. 256°.^{184, 185} The structure is established by oxidation to 4-carboxybenzenephosphonic acid.

2-Thiophenephosphonic acid. XIII. Crystals, m. 159° (from water).²²⁸

9-Acridine phosphonic acid. XIV. Green crystals, m. 247-9° (with decomposition). On standing in hydrochloric acid it is transformed into a yellow form, m. over 350°.¹⁴¹

Diethyl ester. IA. Feathery crystals, m. 165-7°.¹⁴¹

1-Phenyl-5-chloro-3-methyl-1-pyrazolophosphonic acid. XVIII. Plates, m. 191° (from water).²⁰⁵

SECONDARY PHOSPHONIC ACIDS

COMPOUNDS WITH PHOSPHORUS BONDED TO ALIPHATIC CARBON

Me₂PO(OH). X. Hygroscopic crystals that can be sublimed, m. 76°.¹⁰⁸ The 'silver salt forms water-soluble needles, which are somewhat soluble in alcohol and ether.¹⁰⁸

Et₂PO(OH). X.¹⁰⁸ XIII.⁶⁸ XVI.¹⁶¹ Liquid, freezing to needles in freezing mixture: ^{68, 108} b. about 320°.⁶³ Silver salt forms colorless needles.^{108, 161}

Pr₂PO(OH). X. Liquid.¹⁰⁴

Bu₂PO(OH). V.¹⁴⁷ XIII.^{147, 299} Needles, m. 31-2°, ²⁹⁹ m. 70.5-71° (from ligroin).¹⁴⁷

iso-Bu₂PO(OH). X. Liquid.¹⁰⁴

iso-Am₂PO(OH). X. Liquid.¹⁰⁴

MeEtPO(OH). XIII.²²⁰ Needles, m. 45–8° (from water).²²⁰

(PhCH₂)₂PO(OH). IVA.¹⁵⁵ X.^{151, 155} XIII.¹⁵¹ V.^{210, 240} Scales, m. 192°, m. 191°, ^{151, 155} m. 180° (from EtOH).²¹⁰

Methyl ester. XXI. Prisms, m. 75°.¹⁵⁵

(4-O₂NC₆H₄CH₂)₂PO(OH). By nitration of the above acid with fuming nitric acid. Needles, m. 225–6° (from AcOH),⁵⁶ m. 210–2°.¹⁵⁵

(HOCH₂)₂PO(OH). Isolated as the barium salt by boiling (HOCH₂)₄PCl with barium hydroxide. Crystals slightly soluble in water and insoluble in alcohol.¹⁰¹

(Me₂C(OH))₂PO(OH). IVA.^{163, 164, 174} Crystals, m. 185–6° (from EtOH), dec. 150°.^{163, 164} Slowly converted to the corresponding primary phosphonic acid by lead oxide or mercuric chloride. Diacetate, m. 171° (from EtOH); dibenzoate, m. 195–6°.¹⁶⁴

Methyl ester. XXI. Crystals, m. 92°.^{164, 174}

Ethyl ester. XXI. Crystals, m. 95°.^{164, 174}

(PhCHOH)₂PO(OH). IVA.^{174, 253, 257} Needles, dec. 165°, m. 230° (on rapid heating).¹⁷⁴ Diacetate: crystalline solid.²⁵⁷

Ethyl ester. XXI. Prisms (from EtOH).^{253, 257}

(2-HOC₆H₄·CHOH)₂·PO(OH). IVA. Grainy solid, which decomposes without having a true melting point.²⁵⁷

(4-iso-PrC₆H₄·CHOH)₂PO(OH). IVA. Crystals, m. 140°.^{255, 257}

(HOCH₂)(PhCHOH)PO(OH). IVA.^{173, 174} Crystals, m. 154°.^{173, 174}

(MeCHOH)(PhMeCOH)PO(OH). IVA. Crystals, m. 192° (from EtOH-Et₂O).^{173, 174}

(Me₂COH)(PhCHOH)PO(OH). IVA. Plates, m. 182° (from Me₂CO).^{173, 174}

(MeEtCOH)(PhCHOH)PO(OH). IVA. Crystals.^{170, 174}

(MePrCOH)(PhCHOH)PO(OH). IVA. Crystals, m. 170° (from Me₂CO).^{173, 174}

(Et₂COH)(PhCHOH)PO(OH). IVA. Plates, m. 192°.^{173, 174}

(iso-BuCHOH)(PhCHOH)PO(OH). IVA. Crystals, m. 203–5° (from water).¹⁷³

(iso-BuCHOH)₂PO(OH). IVA.^{174, 254, 257} Needles, m. 230° (on rapid heating),¹⁷⁴ dec. 160° (on slow heating).²⁵⁷

(n-C₆H₁₃CHOH)₂PO(OH). IVA. Plates, m. 160° (from EtOH). Diacetate: needles, m. 94°.²⁵⁷

(Me₂COH)(MeCHOH)PO(OH). IVA. Crystals, m. 132° (from Me₂CO).^{173, 174}

(Me₂COH)(n-C₆H₁₃CHOH)PO(OH). IVA. Plates, m. 131° (from Me₂CO).^{173, 174}

(MeEtCOH)(n-C₆H₁₃CHOH)PO(OH). IVA. Crystals, m. 147°.^{173, 174}

(Me·CO·CH₂·CMe₂)BuPO(OH). IVB. Isolated as a hygroscopic potassium salt, after treatment with potassium hydroxide.²³

(PhCO·CH₂·CHPh)BuPO(OH). IVB. Crystals, m. 191–3° (from dioxane).²³

COMPOUNDS WITH PHOSPHORUS BONDED TO AN AROMATIC NUCLEUS

PhMePO(OH). IF.^{194, 221} XIV.⁹ Needles, m. 133°.⁹ m. 134°.²²¹ m. 133–4° (from EtOH).^{194, 221} Menthylamine salt, m. 188–9°; cinchonine salt, m. 170–2°; cinchonidine salt, m. 154°; quinine salt, m. 164–6°.²²¹

Methyl ester. IA.^{9, 23} XV.^{9, 23, 23} Liquid, b₁₅ 141–1.5°.⁹ b₁₄ 141.75°.²³ b₁₃ 137.2–8.2°.²³ b₁₁ 137°.²³ d₀¹⁵ 1.1752°.⁹ d₀¹⁵ 1.1669°.²³ d₀¹⁵ 1.1572°.⁹ d₀²⁰ 1.1575°.⁹ d₀²⁵ 1.1436°.²³ n_D¹⁵ 1.5230°.⁹ n_D²¹ 1.5220°.^{23, 5} n_D^{25.5} 1.4898°.²³

Ethyl ester. XV. (By warming the acid with thionyl chloride, followed by treatment with ethanol.) Liquid, b₁₁ 143° d₄²⁰ 1.107°.²³

PhEtPO(OH). XIV. Plates, m. 79–80° (from Et₂O).^{9, 23}

Ethyl ester. IA. Liquid, b₁₆ 162–4°.^{9, 23}

PhPrPO(OPr). IA. Liquid, b₁₄ 163°.⁹ d₀¹⁵ 1.0591°.⁹ d₀¹⁵ 1.0463°.⁹ n_D^{22.5} 1.4979°.²³

Ph(iso-Pr)PO(OH). XIV. Crystals, m. $61-2^{\circ}$.²⁴

Isopropyl ester. IA. XV. Liquid, b_{11} $146-7^{\circ}$, d_0^{20} 1.0957, d_0^{17} 1.0813, n_D^{20} 1.4929.²⁴

Ph(iso-Bu)PO(OH). IA (spontaneously in the synthesis of isobutyl ester at 160°).¹⁵ XIV.⁸ Crystals, m. $64-5^{\circ}$.¹⁵

Isobutyl ester. IA. Liquid, b_{12} $167-8^{\circ}$.⁸

Ph(Ph₃C)PO(OH). XIV. Crystals, m. $287-8^{\circ}$.¹⁵

Isobutyl ester. IA. Undistillable mass.¹⁵

Ph(Cl₃C)PO(OH). The free acid has not been prepared.

Methyl ester. IA. Crystals, m. 108° .^{124, 125}

Ethyl ester. IA. Crystals, m. 79° , b_1 $147-8^{\circ}$.^{124, 125}

Propyl ester. IA. Liquid, b_1 $150-2^{\circ}$, d_0^{14} 1.3078, d_0^{14} 1.2918, n_D^{19} 1.4945.^{124, 125}

Isobutyl ester. IA. Liquid, b_1 $155-6^{\circ}$, d_0^{13} 1.2861, d_0^{13} 1.2697, n_D^{18} 1.4993.^{124, 125}

Ph(HO₂C·CH₂)PO(OH). XIV. Crystals, m. $121.5-2.5^{\circ}$.¹² Cinchonine salt, m. $195-6^{\circ}$; ammonium salt, m. 215° .¹²

(C)-Ethyl (P)-isobutyl ester. IA. Liquid, b_7 $195-8^{\circ}$, d_0^{10} 1.1223.¹²

Ph(HO₂C·CHMe)PO(OH). XIV. Crystals, m. $168-9^{\circ}$.¹²

(C)-Ethyl (P)-isobutyl ester. IA. Liquid, b_7 $191-3^{\circ}$, d_0^{10} 1.10535.¹²

Ph(MeOCH₂)PO(OEt). IA. Liquid, b_2 $138-9^{\circ}$, d_0^{10} 1.1543, $n_D^{20.5}$ 1.4891.³³

Ph(EtOCH₂)PO(OEt). IA. Liquid, $b_{2.5}$ 149.5° , d_0^{10} 1.1017, d_0^{25} 1.0811, n_D^{25} 1.4910.³³

Ph(MeCHOH)PO(OH). IVB. Needles, m. 104° (from water).¹⁸⁴ The ethyl and isopropyl analogs, prepared similarly, are crude oils.¹⁸⁴

Ph(Me·CO·CH₂·CMe₂)PO(OH). IV (from phenyldichlorophosphine and acetone in the presence of phosphorus pentoxide). Plates, m. 86° (from water; monohydrate).¹⁸³ The silver salt is soluble in water.¹⁸³

Ph(Ph·CO·CH₂·CHPh)PO(OH). IVB. Crystals, m. $220-5^{\circ}$ (from AcOH).⁷⁴

Ph(Ph·CO·CHBr·CHPh)PO(OH). By bromination of the above acid in hot acetic acid or by addition of bromine to the intermediate anhydride (in IVB preparation of the above acid using acetic anhydride). Obtained in two apparently stereoisomeric forms: m. 195° (from EtOH) and m. $160-80^{\circ}$ (from CHCl₃-ligroin).⁷⁴

Ph(PhCH·CH·CO·CH₂·CHPh)PO(OH). IVB. Crystals, m. $235-6^{\circ}$ (from AcOH).⁶⁸ Ozonization of this acid yields Ph(HO₂CCH₂·CHPh)PO(OH), m. 212° (from water).⁶⁸

Ph(Ph·CHBr·CHBr·CO·CH₂·CHPh)PO(OH). By bromination of the above acid. Crystals, dec. 195° (from AcOH).⁶⁸

Ph(Ph·CH·CBr·CO·CH₂·CHPh)PO(OH). By treatment of the above acid with hot methanolic potassium acetate. Crystals, m. 200° .⁶⁸

Ph·CO·CH₂·CH(PhPO₂H)·CH·CH·Ph. IVB. Crystals, m. 200° (from AcOH).⁶⁸

Ph(Ph·CHOH)PO(OH). IVB. Powder, m. $112-4^{\circ}$ (from Et₂O).¹⁸⁴

(4-BrC₆H₄)PhPO(OH). XIII. Crystals, m. 174.5° (from EtOH).⁷⁴

Me(4-MeC₆H₄)PO(OH). IF. Needles, m. 120° .¹⁸⁷

(Me·CO·CH₂·CMe₂)(4-MeC₆H₄)PO(OH). IVB (in the presence of phosphorus pentoxide). Plates, m. $102-3^{\circ}$ (from water).¹⁸³

Ph(4-MeC₆H₄)PO(OH). XIII. Needles, m. 116° .¹⁸⁵ Nitration with fuming nitric acid forms a dinitro derivative, m. 205° .¹⁸⁵

(PhCH₂)(4-MeC₆H₄)PO(OH). XIV. Needles, m. 145° (from EtOH).¹⁸⁵

Phenyl ester. IA. Crystals, m. 120° (from dil. EtOH).¹⁸⁵

Ph(2,4,5-Me₃C₆H₂)PO(OH). XIII. Needles, m. 181° (from EtOH).¹⁸⁵ Phenylhydrazine salt, m. 140.5° ; copper and cobalt salts are soluble in moist ether.¹⁸⁵

170 ACID DERIVATIVES WITH CARBON TO PHOSPHORUS LINK

Cold fuming nitric acid yields a trinitro derivative, m. 197–8°, the silver salt of which is soluble in alcohol and ether.¹⁸⁵

Ph₂PO(OH). V.^{51, 94, 95, 134, 210, 240} X.^{81, 192} XII.^{6, 180, 192, 193, 199} XIII.^{180, 199} XIV.^{149, 197} XV (as by-product).^{6, 7, 8} XVI.^{132, 159, 161} Needles, m. 195–6°, ^{6, 7, 8} m. 191°, ⁹⁵ m. 190–1°, ²¹⁰ m. 190–2°, ¹³⁴ m. 190.5–2°, ¹⁴⁹ m. 188–90°, ¹⁶¹ m. 190°, ^{132, 180, 169, 199}

Ethyl ester. III.¹⁴⁹ IA.¹⁹³ Crystals, m. 165°, ¹⁹³ b_{1.5} 195–6°, ¹⁴⁹ b_{1.5} 173–5°. ¹⁴⁹

Iso-propyl ester. IA.⁶ Crystals, m. 95–6° (from EtOH).⁶

Iso-butyl ester. IA. Crystals, m. 77° (from EtOH).⁶

Phenyl ester. XV. XI. Needles, m. 135–6°. ¹⁹⁹

3,3'(?)-(O₂NC₆H₄)₂PO(OH). By nitration of the above acid with mixed acid. Yellow crystals, m. 268° (from AcOH).³¹ Reduction by means of tin and hydrochloric acid yields the corresponding diamino derivative: brown solid, dec. 276°, which is sparingly soluble in water.³¹

(2-ClC₆H₄)₂PO(OH). XIII. Needles, m. 212–4°. ²²⁹

(4-ClC₆H₄)₂PO(OH). V.¹³⁴ XIII.²²⁹ XIV.¹⁴⁹ Crystals, m. 208–10°, ²²⁹ m. 133–5° (from dil. EtOH).¹⁴⁴

Ethyl ester. III. Solid, m. 75–7° (from ligroin),¹⁴⁶ b_{1.5} 182–3°, (supercooled) ²⁵ n_D 1.5852. ¹⁴⁹

(4-ClC₆H₄)(4-H₂NC₆H₄)PO(OH). By heating the above acid with ammonium hydroxide to 150° in the presence of cuprous oxide. Crystals, dec. 196°. ¹⁴⁶

(4-H₂NC₆H₄)₂PO(OH). As a by-product in the above preparation. Crystals, m. 216–7°, separated from the above by fractional precipitation from acid solution.¹⁴⁶

(3,4(?)-Cl₂C₆H₃)₂PO(OH). Free acid has not been reported.

Ethyl ester. III. Liquid, b_{1.5} 210–5°, ²⁵ n_D 1.5957. ¹⁴⁹

(2-MeOC₆H₄)₂PO(OH). V. Needles, m. 227–8° (from dil. EtOH).¹⁴⁷

(4-MeOC₆H₄)₂PO(OH). V. Needles, m. 179–80° (from dil. EtOH).¹⁴⁷

(4-Me₂NC₆H₄)₂PO(OH). VIII. XI. Crystals, m. 249° (from ligroin-MeOH); unstable in mineral acids.³²

(4-Et₂NC₆H₄)₂PO(OH). VIII. Crystals, m. 253° (on block), m. 195° (capillary), (from benzene-alcohol). Dihydrochloride, crystals, m. 185°. ³²

(2-MeC₆H₄)₂PO(OH). V.²¹⁰ XIII.²²⁹ Plates, m. 101° (from water).²²⁹

(4-MeC₆H₄)₂PO(OH). V.^{147, 210} XIV.¹⁴⁹ Needles, m. 131–2°, ¹⁴⁷ m. 130–2°. ²¹⁰

Ethyl ester. III (obtained as isomer mixture). Liquid, b_{1.5} 176–82°. ¹⁴⁹ The free acid has been also obtained by XIII. In this instance the product, m. 135°. ^{135, 229} Nitration with fuming nitric acid yields a dinitro derivative (possibly 3,3'-), yellow needles, m. 194°. ¹⁸⁵

(4-MeC₆H₄)(4-HO₂CC₆H₄)PO(OH). By oxidation of the above acid with permanganate. Crystals, m. above 300°. ¹⁸⁶

(4(?)-EtC₆H₄)₂PO(OH). XII (as a by-product in the isolation of the aryl-dichlorophosphine obtained by the Friedel-Crafts method). Yellow oil.¹⁸⁴ The copper salt is soluble in moist ether and in alcohol, but insoluble in dry ether.¹⁸⁴

(2,4,6-Me₃C₆H₂)₂PO(OH). XII–XIII (as a by-product in the isolation of aryl-dichlorophosphine; see above). Needles, m. 202–3° (from EtOH).^{184, 185} The cobalt, lead, and nickel salts are soluble in moist ether. Oxidation with permanganate yields a dicarboxylic acid, m. 185° (from hot water).¹⁸⁴

(4(?)-iso-PrC₆H₄)₂PO(OH). XII–XIII. (Obtained as a by-product; see above.) A very high-melting powder.¹⁸⁴

(1-C₁₀H₇)₂PO(OH). V.^{210, 240} XIII (as a by-product; see above).¹⁸⁶ XIII.²³⁹ Needles, m. 202–4°, ¹⁸⁵ m. 205–6°, ²³⁹ m. 220°. ²⁴⁰

Dicamphorylphosphonic acid. Modified XII (by treatment of sodio derivative of camphor with phosphorus trichloride, followed by hydrolysis, after several hours' standing). Crystals, dec. 283° (from EtOH).²¹⁵

Di-2-pyrrylphosphonic acid. V. Solid, which does not melt (from EtOH).²¹³

Di-3-indolylphosphonic acid. V. Crystals, m. 190° (from EtOH).²¹³

Di-2-methyl-3-indolylphosphonic acid. V. Crystals, m. $159-60^{\circ}$.²¹³

5,10-Dihydro-10-phenophosphazinic acid. XI. Plates, which do not melt at 250° (from EtOH).²⁴¹ Fuming nitric acid yields a yellow nitro derivative.²⁴¹

Methyl ester. XXI. Yellow plates, m. $112-4^{\circ}$ (from EtOH).²⁴¹

Ethyl ester. XXI. Plates, m. 99° (from EtOH).²⁴¹

SECONDARY PHOSPHINOUS ACIDS: R_2POH

Only a few, isolated, members have been isolated in the free state. The usual form isolated is the ester R_2POR .

MeEtPOEt. XV. Liquid, b_{15} $67-70^{\circ}$.²²⁹

Et₂POEt. XV. Liquid, b_{15} $80-5^{\circ}$.²²⁹

Pr₂POEt. XV. Liquid, b_{15} $97-103^{\circ}$.²²⁹

Bu₂POEt. XV. Liquid, b_{15} $112-6^{\circ}$.²²⁹

MePhPOEt. XV. Liquid, b_{15} $125-30^{\circ}$.²²⁹

EtPhPOEt. XV. Liquid, b_{15} $137-42^{\circ}$.²²⁹

Ph₂POMe. XV.³⁰ Liquid, b_{10} $151-2^{\circ}$, d_4^{15} 1.1040, n_D^{20} 1.6030; CuCl salt, m. $135-6^{\circ}$.³⁰

Ph₂POEt. XV.^{6,8} Liquid, b_{14} 179° , d_4^0 1.0896; CuI salt, m. $190-1^{\circ}$.^{6,8}

Ph₂POCH₂CH:CH₂. XV. Undistillable without isomerization; CuCl salt, m. $101-3^{\circ}$.³⁰

Ph₂POPPr-iso. XV. Liquid, b_{17} $185-9^{\circ}$,⁶ b_8 160° ,^{6,8,11} d_4^0 1.0925; CuI salt, m. $114-5^{\circ}$.⁶

Ph₂POBu-iso. XV. Liquid, b_{15} 188° (?),³² b_{11} $202-3^{\circ}$,⁶ d_4^{17} 1.0311.⁶

Ph₂POCH₂Ph. XV. Undistillable without isomerization. CuCl salt, m. $125-6^{\circ}$.³⁰

Ph₂POPh. XV. Liquid, b_{22} $265-70^{\circ}$, d_4^{24} 1.140.¹⁹⁷

(2-MeC₆H₄)₂POEt. XV. Liquid, b_{15} $176-85^{\circ}$.²²⁹

Ph(4-MeC₆H₄)POEt. XV. Liquid, b_{15} $180-90^{\circ}$.²²⁹

(4-MeC₆H₄)₂POEt. XV. Liquid, b_{15} $190-5^{\circ}$.²²⁹

(2-ClC₆H₄)₂POEt. XV. Crystals, m. $26-9^{\circ}$, b_{15} $132-7^{\circ}$.²²⁹

(4-ClC₆H₄)₂POEt. XV. Needles, m. $53-60^{\circ}$, b_{15} $169-72^{\circ}$.²²⁹

(4-Me₂NC₆H₄)₂POH. VIII. Crystals, m. 169° (from benzene);³² dihydrate, m. 165° (from water).²⁴⁴

5,10-Dihydro-10-phenophosphazinous acid. XXIV. Needles, shrink at $215-6^{\circ}$ (from dil. EtOH).^{207, 241}

Ethyl ester. XV. Yellow plates, m. $151.5-52^{\circ}$ (from EtOH).²⁴¹

SULFUR-CONTAINING DERIVATIVES

PRIMARY THIOPHOSPHINOUS ACIDS: $RPSH_2$ (OR $RPH(SH)$)

PhPSH₂. XIX. By heating phenylphosphine with an equivalent amount of sulfur in inert atmosphere; besides some Ph_3P_2S , which appears to be the lowest addition product of sulfur to a phosphine. Malodorous oil, which is unstable in hot water. On heating yields phenylphosphine and $Ph_2PS:PS$; the latter is also obtained from phenyldichlorophosphine and hydrogen sulfide.¹²³

172 ACID DERIVATIVES WITH CARBON TO PHOSPHORUS LINK

DITHIOPHOSPHONOUS ACIDS: RPS_2H_2

No free acids have been reported. Their esters are listed.

PhPS₂H₂. Free acid unknown.

PhP(SET)₂. XV. Liquid, $b_{3.5}$ 143–4°, d_0 1.1417.²²

PhP(SBu-iso)₂. XV. Liquid, $b_{12.5}$ 191–2°, d_0 1.0636.²²

SECONDARY THIOPHOSPHINOUS ACIDS: R_2PSH

The free acids have not been reported. Only the esters of the diphenyl derivative are listed below: Ph₂PSR.

Ethyl ester. XV. Liquid, b_{13} 196.5–97°, d_0 1.133.^{7,8}

Propyl ester. XV. Liquid, b_{23} 229–30°.^{7,8}

Allyl ester. XV. Undistillable without isomerization.³⁰

Isobutyl ester. XV. Liquid, b_8 200.5–201°, d_0 1.0892.^{7,8}

Isoamyl ester. XV. Liquid, b_{12} 219–20°, d_0^{17} 1.0645.^{7,8}

Benzyl ester. XV. Liquid; undistillable without isomerization.³⁰

THIOPHOSPHONIC ACIDS: RPSO_2H_2

iso-AmPSO₂H₂. XIII. Crude oil.⁹⁷

(O,O)-Diethyl ester. XV. Liquid, b . 250–5°, d^{20} 0.9848.⁹⁷

PhPSO₂H₂. XIII. Very unstable oil; the potassium salt forms unstable needles.

Attempted conversion to the lead salt removes all sulfur from the compound and yields RPO_3H_2 and RPO_2H_2 , besides lead sulfide.^{132, 196}

(O,O)-Diethyl ester. XV. Undistillable oil, d^{15} 1.12.^{132, 196}

(O,O)-Di-isobutyl ester. XIX. Liquid, b_{10} 181°.⁸

(O,O)-Diphenyl ester. XV. Undistillable oil.^{132, 196}

DITHIOPHOSPHONIC ACIDS: RPS_2OH_2

EtPS₂OH₂. VII. Unstable oil. The nickel salt is a blue-violet solid.¹⁶¹

iso-PrPS₂OH₂. VII. Unstable oil. The nickel salt is a violet solid, dec. 167–9°.¹⁶¹

C₆H₁₁PS₂OH₂. VII. Unstable oil. Nickel salt is a blue solid.¹⁵⁸

PhPS₂OH₂. VII.¹⁶¹ XIV (from PhPS(SET)₂).²² Unstable solid.¹⁶¹

Nickel salt: blue-violet solid, dec. above 200°.¹⁶¹

Sodium salt: crystalline solid.²²

(O-?)-Monomethyl ester. XV. Isolated as the nickel salt, m. 155°.¹⁶⁰

(O-?)-Monoethyl ester. XV. Isolated as the nickel salt, m. 180°.¹⁶⁰

TRITHIOPHOSPHONIC ACIDS: RPS_3H_2

C₆H₁₁PS₃H₂. Isolated as a brown nickel salt by the action of 5% acetic acid upon $\text{R}_2\text{P}_2\text{S}_5\text{Ni}$,¹⁵⁸ obtained by VII.¹⁵⁸

PhPS₃H₂. The free acid has not been isolated satisfactorily.

Diethyl ester. XIX. Liquid, $b_{3.5}$ 191–2°, d^0 1.2201.²²

Di-isobutyl ester. XIX. Liquid.²²

SECONDARY THIOPHOSPHONIC ACIDS: R_2PSOH

Et₂PSOH. V. Plates, m. 76° (from ligroin).²⁴⁶

Ph₂PSOH. Free acid has not been reported.

(S)-Ethyl ester. IA (by-product from Ph₂PSET).^{7,8} Crystals, m. 72–3° (from Et₂O).^{7,8}

(O-?)-Phenyl ester. XIX. Needles, m. 124° (from EtOH).¹⁹⁷

EtPhPSOH. XIV. Isolated as a crystalline sodium salt from sodium ethoxide reaction with EtPhPS(SET). The free acid is oily.²²

- (HO₂CCH₂)PhPSOH.** 1A (combined with XIV, from crude isobutyl ester). Free acid: oil. Sodium salt: crystals.²²
- (HO₂CCH₂CH₂)PhPSOH.** XIV. Oil. Disodium salt: crystals,²² obtained by hydrolysis of the corresponding R₂PS(SBu-iso).²²
- Ph(PhCH₂)PSOH.** XIV (from the dithio ester). Crystals, m. 173–4°.²²
- (PhCH₂)₂PSOH.** V. Plates, m. 171° (from AcOH).²⁴⁶
- Ph₂PSe(OPh).** XIX. Needles, m. 114–5°.¹⁹⁷
- (4-MeC₆H₄)₂PS(OEt)(?).** XV. Crystals, m. 41–2°.¹⁶⁶
- (4-MeC₆H₄)₂PS(OPh)(?).** XV. Crystals, m. 135°.¹⁸⁵

SECONDARY DITHIOPHOSPHONIC ACIDS: R₂PS₂H

- Me₂PS₂H.** VII. XIX. Crystals, m. 47–50°.¹⁵⁸ Unstable in air, soluble in alkalis. Nickel salt: solid, decomposes before melting. Ammonium salt is insoluble in Et₂O.¹⁵⁸
- Et₂PS₂H.** VII.^{158, 159, 161} XIX.¹⁶⁵ In XIX, the addition originally yields a perthio derivative: Et₂PS₂·S·S₂PET₂, m. 105°, which on boiling with ammonium sulfide yields the ammonium salt of the acid, m. 193°. The free acid is an oil.^{106, 161} Silver salt: needles, insoluble in alcohol. Nickel salt: violet solid, m. 110° (if prepared by VII at low temperature), or m. 140.5° (if prepared by VII at 120° or by XIX).¹⁶¹ Cadmium salt: solid, m. 114°.¹⁶¹ The acid or its salts, on treatment with iodine, form an oily analog of phosphatogens (*see* Phosphates): Et₂PS₂·S₂PET₂.¹⁶¹ Benzyl ester. XXI. Crystals, m. 54°.¹⁰⁵
- iso-Pr₂PS₂H.** VII. Nickel salt: violet solid obtained in two forms, m. 122° and m. 190° (from EtOH).¹⁶¹
- iso-Bu₂PS₂H.** VII. Nickel salt: unstable violet solid.¹⁵⁸
- (C₆H₁₁)₂PS₂H.** VII. Oil. Nickel salt, blue violet solid, m. 212° (with decomposition),¹⁵⁸ readily forms a thioanhydride or a salt of the primary acid, having the composition corresponding to R₂P₂S₆Ni, insoluble solid, m. 90–120°.¹⁵⁸
- EtPhPS(SEt).** 1A. Liquid, b_{3,5} 169–70°, d⁰ 1.1693.²²
- Ph₂PS₂H.** XIX.^{158, 159} VII.¹⁶¹ XIII.¹⁵⁸ Crystals, m. 25–30°.¹⁶¹ Nickel salt, m. 173°.^{158, 161} The thioanhydride of this acid is obtained as a thiophosphide: Ph₂PS₂P (possibly: Ph₂PS·P·S), an oil obtained by passage of hydrogen sulfide into hot phenyldichlorophosphine. As a by-product, the true thioanhydride, Ph₂PS·S·SPPH₂, m. 192–3°, is obtained.¹³²
- Ph(PhCH₂)PS₂H.** The free acid has not been obtained, but its phosphatogen, R₂PS₂·S₂PR₂, m. 145–6°, is obtained as the by-product in the preparation of esters (*see* below).²²
- Ethyl ester. 1A. Liquid, b₃ 210–8°, d⁰ 1.1826.²²
- Isobutyl ester. 1A. Liquid, b₁ 145–6°.²²
- Ph(HO₂CCH₂)PS(SBu-iso).** 1A. Undistillable oil.²²
- Ph(HO₂CCH₂CH₂)PS(SBu-iso).** 1A. Liquid, b_{4,5} 200–6°.²²
- (4-MeC₆H₄)₂PS₂H.** The free acid could not be obtained by XIII. Hydrolysis of R₂PSCl by water at 130–40° yields only a pyroderivative, apparently (R₂PS)₂O, m. 165–6° (from EtOH).¹⁸⁵

ARSENIC ANALOGS OF PHOSPHONIC ACIDS

Only the ester forms have been isolated.¹²⁶

- (EtO)₂P(O)AsEt₂BuI.** 1A (from IASuEt). Crystals, m. 182–3°.¹²⁶
- (EtO)₂P(O)AsEtBu.** IB. Liquid, b₁ 112–3°, d⁰ 1.2054, d¹⁴ 1.1865.¹²⁶

(EtO)₂P(O)AsEtAm-iso. IB. Liquid, b₁ 118–20°, d₀⁰ 1.2858, d₀¹⁴ 1.2718.¹²⁶
 (EtO)₂P(O)AsEtPh. IB. Liquid, b₁ 144–5°, d₀⁰ 1.2869, d₀¹⁴ 1.2734.¹²⁶
 (EtO)₂P(O)AsPh(CH₂CH:CH₂). IA. IB. Liquid, b₁ 142–3°, d₀⁰ 1.2568.¹²⁶
 (EtO)₂P(O)AsPh₂. IB. Liquid, b₁ 176–7°, d₀⁰ 1.2971, d₀¹⁶ 1.2845.¹²⁶
 (EtO)₂P(O)AsBuPh. IA. Liquid, b₁ 162–3°, d₀⁰ 1.2411, d₀¹⁷ 1.2345.¹²⁶

TIN ANALOGS OF PHOSPHONIC ACIDS

Me₃SnPO(OMe)₂. IA. Crystals, m. 96° (from EtOH).³⁷
 Et₃SnPO(OEt)₂. IA. Liquid, b_{2.5} 210–20°, n_D¹⁴ 1.4853.³⁷
 Me₂Sn(PO(OMe)₂)₂. IA. Prisms, m. 245–7° (from BuOH).³⁶
 Et₂Sn(PO(OEt)₂)₂. IA. Prisms, m. 249–51° (from BuOH). This product has the molecular weight of a dimer. IB yields the monomer, m. 173–4°.³⁶
 Pr₃Sn(PO(OPr)₂)₂. IA. Crystals, m. 251–3° (from BuOH).³⁶
 Et₃Sn(PO(OPr)₂)₂. IA. Prisms, m. 262–4° (from BuOH).³⁶
 Me₂Sn(PO(OEt)₂)₂. IA. Glass. If the reaction is conducted at 100° it is possible to isolate the adduct: Me₂Sn((POEt)₃I)₂, unstable crystals, which darken in air.³⁶
 Et₂Sn(PO(OMe)₂)₂. IA. Prisms, m. 263.5–65° (from BuOH).³⁶
 MeSn(PO(OMe)₂)₃. IA. White insoluble solid.³⁶
 Sn(PO(OEt)₂)₂. IA. Viscous yellow mass.³⁶
 MeSn(I)(PO(OEt)₃I)₂(?). IA. Yellow crystals, dec. 161°.³⁶

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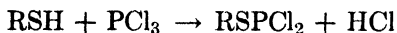
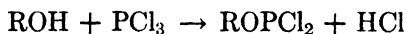
Phosphites and Thiophosphites

The substances included in this chapter are the esters of phosphorous acid, the esters of thiophosphorous acids, and the ester halides of both categories.

SYNTHESIS

I. Reaction of alcohols, phenols, and thiols with phosphorus trihalides and with halophosphites, without tertiary bases

The compounds of the general classes ROPCl_2 , RSPCl_2 , ArOPCl_2 and ArSPCl_2 are obtained by the addition of the appropriate alcohol phenol or thiol to a moderate excess of phosphorus trichloride. The excess of the phosphorus trichloride is useful in the suppression of continued substitution. The mixture of the reagents is subjected to vacuum distillation after the evolution of hydrogen chloride is complete. The reaction with alcohols, especially the lower members, is very vigorous, and cooling must be resorted to; higher alcohols may require mild warming for the completion of the reaction; and phenols require a brief period of refluxing. The over-all reaction may be represented by the formulation.¹²⁰ (Menshutkin; Podkladchikov.)



Similar reaction with phosphorus tribromide serves to form the corresponding bromo analogs. Dihydroxy compounds similarly yield bis-(dichlorophosphites), as demonstrated with the reactions using glycol and dihydroxybenzenes.^{109, 162, 165}

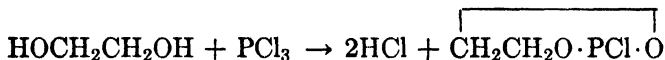
Although the reaction, as represented above, is fairly clean-cut in the aromatic series, it is subject to complications in the aliphatic series, complications that depend on the structure of the alcohol used. The generalization made by Yaroshenko,¹⁸⁰ according to which primary alcohols yield dichlorophosphites, secondary alcohols yield primarily olefins, and tertiary alcohols yield alkyl chlorides, must be taken with reservations. The recent work of Gerrard,⁸⁰⁻⁴ coupled with general considerations of the possible modes of the reaction of phosphorus trichloride or

tribromide, indicates that at least in the instances involving 2-octanol and ethyl mandelate dichlorophosphites are produced. The carefully investigated reaction of methylphenylcarbinol showed that the formation of alkaryl chloride in this instance may take place by means of two mechanisms: "end-on" attack, in which the negatively charged chlorine displaces the hydroxyl group with an inversion of structure, and the "broadside" attack, in which the phosphorus trichloride molecule is oriented along the carbon-oxygen-hydrogen group and the displacement occurs without inversion.⁸²

Triarylcarbinols do not give dichlorophosphites, but do yield their isomerization products, triarylmethylphosphonyl dichlorides, which are considered in Chapter 4.

A notable exception to this reaction is the behavior of 1,2-dihydroxybenzene, which is considered in a later paragraph. Another significant exception is the behavior of benzyl alcohol; the crude dichlorophosphite in this instance invariably explodes on attempted distillation.¹⁵⁷ (Razumov.)

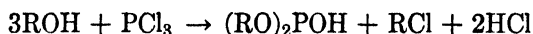
Compounds of the general classes $(RO)_2PCl$ and $(ArO)_2PCl$ are obtained in rather unsatisfactory yields by the extension of the above reaction, using two equivalents of the hydroxy compound. The representation $2ROH + PCl_3 \rightarrow (RO)_2PCl + 2HCl$ serves to illustrate, only in part, the reaction as it occurs in the aromatic series. In the aliphatic series, this procedure generally leads to the formation of poor yields of dialkyl phosphites, $(RO)_2POH$, with the notable exception of the behavior of glycols. These substances, which may be regarded as monomolecular representations of the above equation, produce cyclic chlorophosphites in fair yields, as indicated in the following formulation.^{61, 162} (Arbuzov.)



This reaction, although proceeding apparently by a complex route that is by no means clear after numerous investigations,^{8, 9, 10, 42, 43, 109, 165} is of particular value in the preparation of *o*-phenylene chlorophosphite from 1,2-dihydroxybenzene. This interesting substance may be produced by a variety of techniques, of which the following seem to be the best. The diol is warmed with $1\frac{1}{2}$ moles of phosphorus trichloride until the hydrogen chloride evolution stops at 70 to 80°, after which the mixture is heated briefly to 110° and the warm product is sealed into tubes, kept 4 to 5 hours at 170 to 80°, after which the product is distilled.⁴² The second method makes use of the catalytic action of water on the intermediate products of this reaction, apparently

2-hydroxyphenyl dichlorophosphite in particular, and involves the addition of phosphorus trichloride to the diol in ether containing a small amount of water, followed by warming for 5 hours, standing overnight, and distillation.^{9,10} The action of catalytic amounts of water is not completely clear. It appears, however, to be the activation of halides of trivalent phosphorus, which permits the progress of reactions at low temperatures, otherwise requiring high temperatures for completion. (Anschütz.)

Although the use of still larger amounts of hydroxy compounds, in respect to the amount of phosphorus trihalide, leads to the formation of triaryl phosphites in the aromatic series, in accordance with the over-all formulation, $3\text{ArOH} + \text{PCl}_3 \rightarrow (\text{ArO})_3\text{P} + 3\text{HCl}$, in satisfactory yields, especially when somewhat more than 3 moles of the phenol are used, the aliphatic compounds show a distinct departure from this equation. It is at this point that the old formulation of Wichelhaus¹⁷⁸ breaks down completely. The over-all result of the reaction involving 3, or more, moles of an aliphatic alcohol with phosphorus trihalide is the formation of dialkyl phosphite and alkyl halide, which may be shown by



This reaction is the most convenient method of preparation of dialkyl phosphites, and in its generally applicable form consists of the addition of phosphorus trihalide, preferably trichloride, to the alcohol with appropriate cooling to moderate the reaction. Although solvents, such as carbon tetrachloride and benzene, have been suggested, there seems to be no particular advantage in their use, except in the cases involving the lower alcohols where effective cooling is more difficult. The temperature should be held below 10 to 15° for the methyl and the isopropyl derivatives; other alcohols, particularly the higher members, may be used at somewhat higher temperatures. After the addition of phosphorus trichloride, customarily performed with suitable agitation, the reaction vessel is evacuated, and the hydrogen chloride and the alkyl chloride are removed. The product is then distilled under reduced pressure. The pumping-out of hydrogen chloride and alkyl chloride is usually a lengthy process, requiring several hours. For this reason, it may be advantageous to saturate the reaction mixture, after an initial evacuation, with dry ammonia and to remove the resulting ammonium chloride prior to distillation of the ester.¹¹⁶ The actual distillation must be conducted in good vacuum, and the distillation residue must not be subjected to undue heating if formation of phosphine and related substances is to be avoided. The nature of these residues, which are small

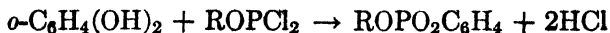
in amount when rigidly anhydrous conditions are used, is not clear, but they appear to consist at least in part of phosphorous acid and mono-alkyl phosphites.

The usual explanation for the formation of dialkyl phosphites is that the trialkyl ester, first formed, is cleaved by hydrogen chloride in the manner indicated by the equation above. This view is supported by experiments with dry hydrogen chloride and the pure esters. It cannot be held, however, that this mechanism has been completely established, and the tenacious retention of hydrogen chloride by the reaction mixture indicates a possibility of the intermediate formation of coordination complexes, which have a finite dissociation pressure. The additive tendency of phosphorus increases with substitution of halogen atoms by alkoxy groups; the product having an appreciable degree of such substitution may be expected to have a fair order of stability. The final proof of the reaction mechanism in this and in other instances in this chapter relating to reactions of hydroxy compounds with phosphorus halides remains to be established.

The use of an aliphatic or an aromatic thiol in the indicated proportions leads to the formation of trithiophosphites, $(RS)_3P$. This reaction requires heating, with disappointing yields for the aliphatic compounds, although the aromatic compounds react fairly satisfactorily.¹¹⁴ (Lippert, Reid.)

Phenols, especially when used in excess, readily yield triaryl phosphites on refluxing with phosphorus trichloride. The compounds of high molecular weight react satisfactorily in the presence of catalytic amounts of magnesium chloride.¹⁴¹

The reaction of glycols with phosphorus trichloride under the deficiency conditions of the trichloride has not been studied adequately. The older work of Carre⁵⁹⁻⁶⁵ is definitely inadequate. With the aromatic analog, 1,2-dihydroxybenzene, the reaction leads to a fair yield of tri-*o*-phenylene diphosphite, among other products. Alkyl and aryl *o*-phenylene phosphites may be formed in rather unsatisfactory yields by heating the appropriate dichlorophosphites with 1,2-dihydroxybenzene.^{13, 42} Although the expected course of the reaction (Anschütz; Arbuzov)



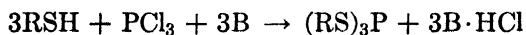
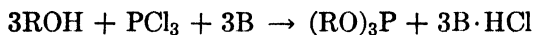
is followed by the reactants, the final reaction mixtures invariably consist of the complete range of disproportionation and translocation products.

In all the reactions described above, as in all instances of derivatives of trivalent phosphorus, careful and precise work should be done in

inert atmosphere. This is particularly true of the very reactive cyclic phosphites and the thio derivatives. Usually carbon dioxide or nitrogen is quite satisfactory.¹⁵⁶ (Arbuzov.)

II. Reactions in the presence of a tertiary base

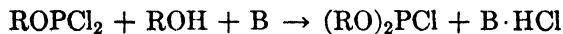
The reaction of phosphorus trihalides, principally trichloride, with hydroxy compounds and with thiols in the presence of a tertiary base is the basis for the most satisfactory preparation of trialkyl phosphites and trialkyl trithiophosphites. The over-all reaction may be represented by the following equation. (Milobendzki.)



The reaction in this form is conducted by the addition of the phosphorus trihalide to the solution of the alcohol (used in slight excess over 3 moles) in an inert solvent, such as ether, petroleum ether, or benzene, containing the corresponding amount of a tertiary base. The base may be a heterocyclic base such as pyridine,¹³⁴ or the rather more readily usable amines like dimethylaniline or diethylaniline.^{77, 159} The reaction is performed with adequate stirring and cooling (usually at about 10 to 15°). After completion, the amine hydrohalide is filtered off and the product is isolated by distillation in vacuum.

A simple modification of this reaction in which the amount of the base is reduced to 2 moles serves to form the dialkyl phosphites that are not readily obtainable by procedure I. Chief among them is dibenzyl phosphite.^{49, 50} (Atherton *et al.*)

The reaction of dichlorophosphites with 1 mole of an alcohol in the presence of an equivalent of a tertiary base is the best preparation available for dialkyl chlorophosphites.^{104, 156}



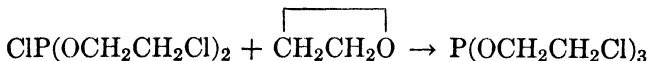
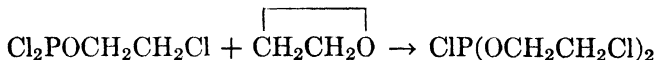
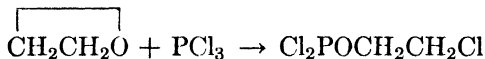
The closely related cyclic monochlorophosphites are also best made by this procedure from the glycols and phosphorus trichloride in the presence of two equivalents of a base.^{44, 162} A simple modification in which phosphorus trichloride is replaced by an alkyl dichlorophosphite readily yields the neutral esters, alkyl alkylene phosphites.^{44, 162} The corresponding thio derivatives are also obtainable by this procedure,⁷³ although the yields are not satisfactory and a good preparation of dialkyl dithiochlorophosphites is as yet unavailable. (Arbuzov; Kabachnik.)

The work of Gerrard, mentioned in an earlier section, should be consulted for the current status of the mechanism of this reaction. The older work^{94, 107} is not sufficiently detailed. The primary function of

the base is the removal of hydrogen chloride, the same products being obtained by the reversal of the customary order of addition.⁸¹

III. Reaction of phosphorus trihalides or halophosphites with cyclic oxides, imines, and sulfides

This reaction serves to produce a variety of dihalophosphites, halophosphites, and trialkyl(aryl)phosphites. Although the reaction proper was mentioned in the patent literature some years ago⁹⁶ with apparent disclosure of the products, the actual investigation of the products conducted by Kabachnik and associates¹⁰⁰⁻⁴ showed that the earlier disclosure was inadequate and in some respects erroneous. The over-all reaction consists of the progressive addition of the oxide (ethylene oxide has been studied in particular) to the phosphorus trihalide, with opening of the oxide ring, as shown below:

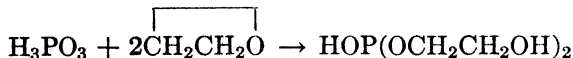


The reaction is conducted simply by passage of the oxide into the trihalide (trichloride or tribromide) until the required gain in weight is achieved. The reaction is highly exothermic, and cooling is essential; approximately 15 to 20° is the optimum temperature for the chloride, whereas -10° or 0° is more satisfactory for the bromide. Although the yield of distillable dihalophosphite is satisfactory, the monohalides are not readily obtained, as they suffer substantial disproportionation on distillation. The neutral esters are quite stable in this respect, but they undergo self-isomerization (discussed in a subsequent section on reactions) during distillation. The triesters, therefore, although obtainable in good yield in the crude reaction mixture, cannot be distilled satisfactorily. (Kabachnik.)

The simple modification of this reaction, in which a halophosphite is used instead of phosphorus trihalide, serves to produce the corresponding mixed esters, although in severely restricted yields owing to a significant extent of transesterification.¹⁰⁰

While it may be expected that the other oxides can behave in the same manner as ethylene oxide, only epichlorohydrin has been studied, and that imperfectly, some years ago.⁹⁰ The rather similar action of cyclic nitrogen and sulfur compounds may be expected. The reaction

of these and of the oxides with phosphorous acid is claimed to lead to the formation of the corresponding amides, thio esters, and esters of phosphorous acid.¹ Unfortunately, no adequate description of the reaction and of the products, outside the patent literature, can be found. The reaction with oxides and cyclic sulfides is given in the following equations, controlled solely by the relative amounts of the reagents used.

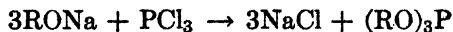


IV. Disproportionation of phosphites and halophosphites

This reaction, which is an undesirable side reaction in many of the usual preparation methods, in the presence or in the absence of tertiary bases, serves a useful purpose in the aromatic series by providing a fairly useful procedure for substances like diphenyl chlorophosphite. Generally a mixture of a neutral phosphite ester and phosphorus trihalide (usually trichloride) undergoes severe disproportionation at mild temperatures (about 50°) in the aliphatic series and at higher temperatures (about 150°) in the aromatic series. The reaction products cover the entire gamut from (RO)₃P to PX₃, and the extent of the formation of any one individual may be controlled within reasonable limits by the ratios of reagents used.^{8, 9, 69, 81} In many respects the mixture may be regarded as a mobile equilibrium system that can shift even during the course of isolation of the products by vacuum distillation. (Anschütz; Gerrard; Conant.)

V. The reaction of alkali alkoxides with phosphorus trihalides or halophosphites

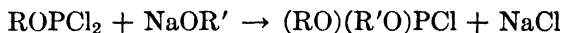
This reaction formed the basis for the classical work of Arbuzov on the preparation and the study of trialkyl phosphites.^{15, 16} The older preparations^{61, 97, 154, 166, 178, 183} resulted in extremely impure materials that caused a considerable divergence of the reported reactions of esters of phosphorous acid. The formation of impure materials is not at all surprising, for this reaction does not lend itself readily to a convenient operative technique. In its classical form it consists of the gradual addition of 1 mole of phosphorus trichloride to a cooled and agitated suspension of 3 moles of alkali (usually sodium) alkoxide in an inert solvent (usually ether). The expected reaction may be shown by



but the actual products isolated from the filtrate (the filtration is in

itself a most tedious task because of the fine particulation of sodium chloride) consist of trialkyl phosphite, dialkyl phosphite, and trialkyl phosphate. The by-products arise in part from alkali, which is usually present to some extent in the alkoxides, and in part from the disproportionation reactions that occur at the point of contact of phosphorus trichloride with the solid alkoxides. The isolation of pure triesters in this procedure is most laborious, and the current trend is toward the procedures given in Section II. Even the original exponent of this procedure, Arbuzov, in his later work appears to have abandoned it.¹⁴⁴

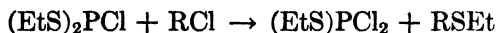
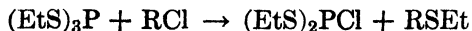
The reaction has been used with moderate success, however, for the synthesis of dialkyl chlorophosphites, especially of the mixed types.^{30, 31, 41, 156} Transesterification, however, severely restricts the yields of the desired products. In the case of diethyl chlorophosphite the reaction is worthless, as the boiling points of the chlorophosphite and the attendant triethyl phosphite are essentially identical. This modification is best done by the addition to the alkyl dichlorophosphite of a suspension of sodium alkoxide in ether or petroleum ether, with cooling.



A reaction of this category was used to prepare phosphites of acetone-glucose from its potassium derivative and phosphorus trichloride.¹⁴² Similarly alkyl phenylene phosphites have been made from sodium alkoxides and the cyclic phenylene chlorophosphite,⁴² although the yields were extremely unsatisfactory.

VI. Displacement of thioalkyl groups by halides

This class of reactions is quite narrowly restricted to the thiophosphites. In its essence it consists of heating trialkyl trithiophosphites or dialkyl chlorodithiophosphites with alkyl or acyl chlorides to 140 to 150°. The reaction results in the replacement of a thioalkyl group by a chlorine atom. Thus the reaction may be represented progressively as follows:



The reaction has been investigated with a variety of halides, but the generally poor stability of halophosphites other than those based on chlorine restricts this reaction as a synthetic method to the chloro derivatives. Usually acetyl chloride or benzyl chloride are used.⁷³ The reaction is represented⁷³ by the successive addition of the reagent to the sulfur atom of one of the thioalkyl groups of the ester, followed by cleavage along the indicated lines. This reaction is most suitable for the preparation of dialkyl chlorodithiophosphites. (Divinskii, Kabachnik.)

VII. Action of halogens on alkali dialkyl phosphites

The reaction of halogens with alkali salts of dialkyl phosphites is a complex process, described in the section on reactions of phosphites. In a specific instance, however, of chlorine and sodium diethyl phosphite, with the reaction being conducted with cooling in inert solvent, a small amount of diethyl chlorophosphite has been obtained.^{30,31} (Arbuzov.)

VIII. Hydrolysis of phosphites

The hydrolysis of trialkyl phosphites with dilute acids or bases under mild conditions is an uneconomical method of preparation of dialkyl phosphites.^{20,127} However, this reaction is a very satisfactory procedure for the preparation of salts of monoalkyl phosphites from dialkyl phosphites. (Arbuzov; Milobendzki; Nylen.)

Although triethyl phosphite and the higher trialkyl phosphites are stable in pure water even at 100°, ^{20,44} trimethyl phosphite is rapidly hydrolyzed to dimethyl phosphite and methanol. The dialkyl phosphites are hydrolyzed rapidly in the presence of catalytic amounts of acids, with the rate curve showing a minimum at the changeover from the essentially hydroxyl catalyzed to the proton catalyzed reaction.¹⁴⁵ Trialkyl phosphites are hydrolyzed very rapidly to the dialkyl esters in the presence of acids, but quite slowly in alkaline solution.²⁰ Hydrolysis of the dialkyl esters, which is of particular interest, occurs with alkaline conditions. Esters like diethyl phosphite lose one ester group so rapidly in alkaline solutions that the rate cannot be measured with any accuracy.¹⁴⁵ By treatment of the dialkyl phosphites with 1 mole of sodium hydroxide in water-alcohol mixtures satisfactory yields of sodium monoalkyl phosphites, $(RO)(NaO)POH$, can be obtained by careful evaporation in vacuum.¹⁴⁶ Moderately good results are obtained by the treatment of sodium dialkyl phosphites with 1 mole of water in dry alcohol, with cooling; the reaction proceeds in two steps, with initial formation of the dialkyl phosphite and sodium hydroxide, followed by the hydrolysis proper.^{99,145,146} (Nylen.)

The tertiary phosphites that contain a cyclic structure (glycol derivatives) generally suffer ring opening on hydrolytic treatment. This usually takes place in a rather vigorous manner. (Arbuzov.)

The higher monoalkyl phosphites may be prepared fairly satisfactorily by treatment of the dialkyl esters with dry hydrogen chloride at 0 to 50°. ⁸²

IX. Hydrolysis of halophosphites

Although the action of water on the halophosphites results in the formation of the corresponding phosphites (primary or secondary), the

isolation of the products from such mixtures is not very satisfactory as a rule because of the continued hydrolysis of the phosphites. Only in the higher members of the class is it feasible to secure moderate yields of the desired esters. The mixture of the mono- and the dialkyl esters is separated in such cases by treatment with sodium carbonate solution in the cold, which dissolves the former compounds; they can be isolated upon acidification. (Gerrard; Kunz.)

In the aromatic series this reaction generally fails because of easy hydrolysis of the esters. Monoaryl phosphites may be isolated upon hydrolysis of the dichlorophosphites in the cold with the theoretical amount of water, which is followed by evaporation in vacuum. Any appreciable excess of water causes complete hydrolysis.¹¹¹ Only a few such compounds have been successfully isolated.

X. Reaction of alcohols with phosphorous acid

When a mixture of phosphorous acid is warmed with an alcohol, an equilibrium is established between the above substances, on one hand, and monoalkyl phosphite, dialkyl phosphite, and water, on the other hand. The yields of the individual substances are generally poor, with the separations being performed as shown in Section IX.^{20, 163}

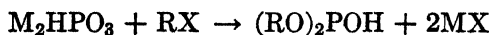
Although the preparation of esters of phosphorous acid with various glycols has been reported, in which the reaction was carried out in vacuum to remove the water, there is little evidence of any homogeneity or individuality of the products obtained.^{59, 65, 115} Rather obviously, dehydration reactions of various types may occur in such a technique with polyhydroxy derivatives.

XI. Reaction of diazo compounds with phosphorous acid

Diazo compounds, as might be expected, smoothly convert phosphorous acid to the corresponding dialkyl phosphites in a reaction that requires 2 moles of the diazo compound per 1 mole of the phosphorous acid.^{49, 150} As a rule, the reaction is of little interest, except for the preparation of special esters, such as dibenzhydryl phosphite,⁴⁹ which are difficult to obtain in a pure state by conventional methods. The reaction is conducted conventionally in dry solvents.

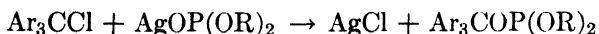
XII. Reaction of metal phosphites with alkyl halides

This reaction is also of narrow interest for the most part. Its use has been widely supplanted by more conventional procedures. In its simplest form it may be represented as



This reaction has been made to serve in the synthesis of a few dialkyl esters by the process of heating a mixture of lead phosphite with the desired alkyl iodide. The reaction gives poor yields, is slow, and requires temperatures in excess of 100°. ¹²²

However, the reaction of alkyl halides with the salts of dialkyl phosphites is of much greater interest. In its usual course it leads to the "isomerization" reactions (see General Characteristics in this chapter), but a few special cases result in an unusual synthesis of triesters of phosphorous acid. Triarylmethyl chlorides react with silver dialkyl phosphites to form the corresponding dialkyltriarylmethyl phosphites, when the reaction is run in an inert solvent at substantially room temperatures. ²² (Arbuzov.)



Similarly, di-isopropyl phosphite in the form of its silver salt yields the corresponding tertiary phosphite with triarylmethyl bromides. In all other cases, the bromides yield the normally expected phosphonates. This instance may be explained by the steric effect of the two bulky isopropyl groups that seem to prevent the reaction from occurring directly at the phosphorus atom.

The results with the chlorides, cited above, have not been explained satisfactorily. It may be added that this reaction conducted without solvent at the melting point of the halide gives the normally expected phosphonates. ²²

XIII. Reaction of alcohols with phosphorus trioxide

This reaction is mostly of theoretical interest at this time. The availability of the necessary trioxide is essentially negligible. However, it may be mentioned that diethyl phosphite was obtained in a moderate yield by the reaction of ethanol with the trioxide in an extremely vigorous reaction, which liberates appreciable amounts of phosphine. ¹⁷⁶ Nothing definite is known about the other by-products, but the reaction probably takes a course similar in most respects to the reaction with the pentoxide, discussed in Chapter 9. It is very probable that the final reaction mixture consists of dialkyl and monoalkyl phosphites and phosphorous acid, essentially. The proportion of dialkylation may be expected to rise with higher alcohol levels. It does not seem probable that any appreciable amounts of tertiary esters can be obtained in this reaction. (Thorpe *et al.*)

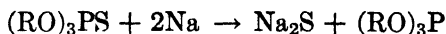
XIV. Hydrolysis of tetra-alkyl pyrophosphites

The pyrophosphites necessary for this reaction are prepared only with considerable difficulty (see Chapter 12). As a result, this method of synthesis of dialkyl phosphites is of little interest at this time. The reaction has been used to demonstrate the nature of these esters. It is conducted by addition of the theoretical amount of the requisite water, as shown by the equation below, to the pyrophosphite. The reaction, which is most vigorous, should be conducted with cooling and with considerable care, especially in larger preparations.⁴¹



XV. Reaction of thionophosphates with alkali metals

This reaction has not been used for synthesis of the esters in the true sense of the word, although there is no evident reason for its limitation to the single instance found in the literature.¹⁵¹ Trialkyl thionophosphates lose their sulfur atom upon treatment with alkali metal (sodium or potassium) on standing. The reaction is probably general for all thiono derivatives. Obviously, it can be used only for the tertiary esters. (Pishchimuka.)

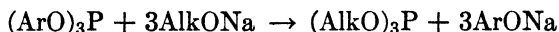


XVI. Transesterification of phosphites

The information on this reaction is quite scanty and confusing. It has been reported that triphenyl phosphite is readily converted to propyldiphenyl phosphite on treatment, under mild conditions, with one mole of sodium propoxide, in an exchange reaction that yields sodium phenoxide.¹³⁶ It is also reported that triaryl phosphites, specifically tricresyl phosphite, react with the higher alcohols (those having boiling points above 100°) by displacement and yield the respective tertiary phosphites in which one or two aryl groups are replaced by the corresponding alkyl radicals.¹⁵⁸ Yet a reaction with propanol and triphenyl phosphite conducted under similar conditions (heating above 150°) has been reported to yield dipropyl propanephosphonate, that is, the isomerization product of the expected phosphite ester.¹³⁶ The reaction in which alcohols as such are used, therefore, needs a careful examination of the actual observable facts, in the most general terms. It may be added that ethyl-*o*-phenylene phosphite yields 2-hydroxy-phenyl-*o*-phenylene phosphite on heating with catechol, in a displacement reaction of this type.¹³ (Milobendzki *et al.*)

The reaction with the sodium alkoxides, however, appears to be rather straight-forward, and may be made to proceed to the replacement

of one, two, or three aryl radicals, depending upon the relative amount of the alkoxide used.¹³⁶ A typical reaction of this type may be shown:



GENERAL CHARACTERISTICS

The halophosphites, which may be regarded as the ester halides of the parent phosphorous acid, combine the properties of the ester and the acid halide functions with those of trivalent phosphorus. They are usually liquids, resembling somewhat the trichloride in their general appearance and behavior. Usually the primary dihalophosphites are substances that are very stable to heat, with the chloro derivatives being best in this respect.⁸¹ The secondary monohalophosphites, on the other hand, are usually but little stable to heat and to prolonged storage. Under either condition, they tend to disproportionate to the dihalophosphite and the tertiary ester, accompanied generally by liberation of small amounts of free phosphorus.¹⁰¹ Although the above remarks are particularly true of the alkyl derivatives, the aryl members of the series show a considerable deviation from this behavior in that they are somewhat more prone to undergo the disproportionation reactions.

The hydrolytic reactions of these compounds were indicated earlier. However, it is well to keep in mind the rough parallel between the halophosphites and the corresponding halophosphines, a parallel that is quite close, except, of course, for the ester hydrolysis that cannot occur in the halophosphines. As such, the halophosphites possess the usually characteristic reactions of trivalent phosphorus and add sulfur or selenium on heating to form the thiono- or selenohalophosphates.^{4, 151} They add halogens in the usual manner to form the quasi-phosphonium derivatives,^{4, 53, 123, 143, 155} which may be converted to the halophosphates by convenient methods.⁷⁴ It is of interest that allyl dichlorophosphite suffers degradation to allyl bromide on treatment with bromine. This compound also undergoes an unusual reaction with two moles of Grignard reagents, a reaction that after the hydrolytic step yields primary phosphonic acids.¹⁵² The alcoholic reactions were discussed in Sections I, V, and XVI devoted to the methods of preparation.

Although concrete information is lacking on the possibility of reactions of the halophosphites with alkyl halides in a manner analogous to the reactions of the tertiary esters, it is possible to predict that the reactivity of the halophosphites would be quite low and would be rather comparable to that of phosphorus trihalides.

The reactions of the thiohalophosphites are rather poorly portrayed. Although, generally speaking, they retain the reactions of the oxygen analogs, the esterification reactions that they undergo are rather more complex. Thus phenyl dichlorothiophosphite undergoes a very substantial dislocation on treatment with alcohols. Among the products obtained are appreciable amounts of thiophenol and of trialkyl phosphites. Reaction with sodium alkoxide yields a mixture of trialkyl phosphite and triphenyl trithiophosphite.

The dihalophosphites react with substances that characteristically replace a pair of halogen atoms by an oxygen atom (such as oxalic acid, see Chapter 4) and form the corresponding metaphosphites.⁷

In common with other derivatives of trivalent phosphorus, the halophosphites form typical double salts with metal halides. Of special interest are the adducts with cuprous halides, which are used for characterization purposes.¹⁷

The esters of phosphorous acid should be examined after division into the three main categories, primary, secondary, and tertiary.

The primary phosphites, ROPO_2H_2 , are generally sirups that show monobasic properties, characteristic of the hydrolysis products of dihalides of trivalent phosphorus. In this respect, a parallel may be drawn between these esters and the phosphonous acids. They may be regarded as existing in the free state in the form of the keto structures, with only one normally ionic hydrogen, $\text{ROP}(\text{O})(\text{OH})\text{H}$. They are undistillable and are usually prepared in the form of the metallic salts.¹⁴⁶ The free acids are stronger than phosphorous acid, in accord with the usual trend upon replacement of the proton by an alkyl radical. They are very resistant to oxidation and are only slowly attacked by bromine in weakly alkaline solutions.¹⁴⁶ Their hydrolysis in acid solutions is unimolecular and is independent of the hydrogen ion or the ester concentrations.¹⁴⁶ It is quite probable that in the free state these esters exist in associated state, through hydrogen bonding, similar to that of the secondary esters.

The secondary esters, $(\text{RO})_2\text{POH}$, are of considerably greater interest both from the historical point of view and from the point of view of practical usefulness. They are essentially odorless liquids (the higher members are low melting solids) that can be distilled in vacuo. They are neutral in the usual sense of the word, in that they do not form salts with bases in the normal manner through the medium of the residual hydrogen atom. However, the salts may be readily prepared by other methods (see below). The prolonged argument about the precise structure of these esters, and in fact the argument about the structure of the parent acid, was clarified substantially by the work of Arbuzov, who showed

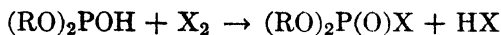
that the esters exist substantially in the keto form, that is, $(RO)_2P(O)H$, in the free state, thus explaining their lack of oxidizability, their lack of the true acidic characteristics, and their inability to add cuprous halides.^{15, 16} Recent studies of these esters by physical methods, principally the parachor measurements and the Raman spectra, showed that the substances exist in the free state in the form of associated, probably cyclic, structures that may be assigned dimer or trimer magnitudes. Such association, best represented by hydrogen bonding, appears to be typical of the phosphorus compounds that have been traditionally given the keto structure with pentavalent central atom. In the light of this information the argument about the enol-keto forms becomes quite meaningless.^{45, 47, 48}

The metal derivatives of these esters, or their "salts," may be prepared in several ways. The alkali metal salts are readily obtained by the direct action of the metal on the ester in a suitable solvent. Thus ether, benzene, hexane, toluene, and similar solvents have been used. The reaction, in which hydrogen is displaced, is usually rather vigorous with the lower members and should be conducted with appropriate care, especially if finely divided metal is used. The alkali salts, principally the sodium salt, are moderately soluble in such solvents when the ester radicals are small; esters of the higher alcohols (butyl and higher) form sodium salts that are freely soluble even in petroleum fractions. The sodium salts may also be prepared from sodium alkoxides, either in the dry state in inert solvents or in situ in the original alcohols.¹⁴⁵ Magnesium salts cannot be made by direct metal action, although they are readily prepared in the presence of pyridine; the higher esters require moderate heating for completion of displacement.¹³⁰ The poorly soluble silver salts of dialkyl phosphites, which form thread-like crystals, may be prepared by the addition of a theoretical amount of ammoniacal silver nitrate solution to an aqueous solution, or suspension, of the ester, followed by very careful neutralization with nitric acid.¹³⁷

A less generally applicable procedure, which fails with the lower esters because of hydrolytic reactions, consists of gradual addition of sodium or potassium hydroxide solution to a mixture of equivalent amounts of the ester and silver nitrate in water.¹³⁷ The preparation that yields completely pure, light-stable silver salts proceeds through suspension or solution of the ester in a large amount of water, addition of a few drops of ammonium hydroxide, and slow addition of the theoretical amount of silver nitrate solution. The first precipitating particles are usually dark and should be filtered off.^{21, 22} Exchange reaction between silver nitrate and the sodium salts may be used to prepare the silver salts, but does not seem to be advantageous over the above method.⁹⁹

The essentially insoluble cuprous salts are prepared by addition of hydrated cuprous oxide to an aqueous solution or suspension of the ester with shaking. The product is separated from the traces of cupric salt and residual cuprous oxide by vigorous stirring and "skimming" the fibrous product from the surface.²¹

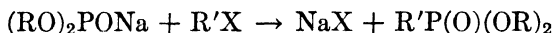
Secondary phosphites enter a number of interesting and useful reactions. Of these, the reaction with the halogens is of special interest in that it affords the most convenient method of preparation of secondary chloro- and bromophosphates. In its essence, the reaction may be shown as follows:



Although it is effective with iodine, the products are too unstable to be actually isolated. The reaction is discussed in more detail in Chapter 9.^{51, 70, 91, 117, 176} The reaction with iodine was studied kinetically,¹⁴⁸ with indication that the rate-determining step is the detachment of the hydrogen that is presumably bound directly to the central phosphorus atom.¹⁴⁵ A recently discovered reaction, which bears some degree of similarity to the above, at least in the sense of forming analogously reacting products, should be mentioned at this point.^{51, 52} Secondary phosphite esters react with aliphatic polyhalides in the presence of a suitable base to form substances that behave like secondary halophosphates, that is, they are capable of forming amidophosphates, etc. The true course of the reaction, and, as a matter of fact, even the nature of the final products, remain somewhat obscure at this time. The two possibilities of formation of either $(\text{RO})_2\text{P}(\text{O})\text{X}$ or $(\text{RO})_2\text{P}(\text{O})\text{CX}_3$ derivatives from carbon tetrahalides (the most effective reagents as a rule) have not been excluded, since the latter class of substances also yields amidophosphates on reaction with amines. It is, however, most likely that the formation of halophosphates, or of structures very similar to them, takes place in this reaction, which is considered in specific cases in Chapter 10. The reaction may be considered primarily as a very mild method of phosphorylation, and it proceeds well with carbon tetrahalides, penta- and hexachloroethanes, bromoform, iodoform, dichlorobromomethane, tetrachlorodibromoethane, and tetrachloroethane (less well). Trichlorobromomethane appears to be the most effective reagent. The base that must be present should be ammonia or a strong primary or secondary amine. Thus aniline ordinarily is not phosphorylated unless a tertiary auxiliary base is present, although the use of trichlorobromomethane gives direct reaction even in the absence of the auxiliary base.^{51, 52}

Although the free dialkyl phosphites do not add sulfur, their alkali metal derivatives do this with great ease and form the corresponding salts of dialkyl thiophosphates.⁷⁸

The metal derivatives of the dialkyl phosphites are extremely useful intermediates for the synthesis of esters of phosphonic acids. In general, these substances react with alkyl halides, or substances that carry a halogen atom on an aliphatic carbon, with the formation of the above phosphonates and the corresponding metal halide. The notable exceptions to this reaction are the special cases of silver derivatives given in Section XII of this chapter, reactions of secondary halides that usually result in twinning of the organic radical of the original halide and the concurrent formation of $(\text{RO})_2\text{PO}$ radicals, and the as yet unclarified reactions with acyl halides. Ordinarily, the sodium derivatives are used in this reaction, which may be shown as



Reactions of this type have long been used as an argument for the keto structure of the metal derivatives. Studies of the X-ray spectra of the metal derivatives in the solid state indicate that the sodium derivatives are in the keto state, that is, the metal appears to be phosphorus-bound, whereas the silver derivatives appear to have the enol structure, with $-\text{OAg}$ linkage.¹⁶⁹ However, the conditions existing in the solid state may not be in correspondence with the conditions in solution in the course of reaction, as is clearly shown by the different types of products obtainable from the silver salts, depending upon the conditions used. In any explanation of the radical transfer that takes place in these "isomerization" reactions account must be taken of the fact that the interaction of the organic halides with the metal dialkyl phosphites invariably leads to but one type of product, either a phosphonate or a phosphite, but never a mixture of the two.²¹

The tertiary esters, $(\text{RO})_3\text{P}$, are perhaps the most reactive substances in this class. As true derivatives of trivalent phosphorus they undergo the usual addition reactions: formation of cuprous halide salts, addition of sulfur to yield tertiary thionophosphates, oxidation (under mild and anhydrous conditions) to the corresponding phosphates, etc. A notable exception to the sulfur addition rule is shown by *o*-phenylene-2-hydroxyphenyl phosphite, which does not add sulfur. It is possible that association of the ortho group with phosphorus is the cause.¹⁸ The reactions of alkyl members with arylmagnesium halides yield diaryl-alkylphosphine oxides (see Chapter 6) whereas the aryl members yield tertiary phosphines (see Chapter 2).

The tertiary phosphites undergo the Michaelis-Arbuzov reaction with organic halides of the same types that were indicated above for a similar reaction of the metal derivatives of dialkyl phosphites. On the whole, the tertiary esters enter this reaction with less deviation from the normal formation of the phosphonate esters than is shown by the derivatives of the dialkyl phosphites; the formation of phosphites does not take place. The reaction, which may be given the scheme



proceeds normally with a very wide range of substances. It is discussed in more detail in Chapter 7. At this time it may be pointed out that, in addition to the usual organic halides, the reaction is successful with substances like organotin halides,^{34,46} cyanogen iodide,¹⁶⁴ and the triaryl-methyl halides. The last reaction is decidedly different from the action of triarylmethyl bromides upon sodium dialkyl phosphites, which results in the formation of free triarylmethyl radicals and the phosphite radical $(\text{RO})_2\text{PO}\cdot$, mentioned earlier.^{24,26} If radical R' is identical with radical R , the reaction becomes a true isomerization, for catalytic amounts of the reagent are necessary to carry on the reaction chain.^{15,16} The notable failures of the reaction may be given as follows. The nitro compounds, such as nitrohaloalkanes or nitrobenzyl halides, lead to oxidation of the phosphite and do not yield the phosphonates.³² Aryl-sulfonyl chlorides or alkyl chlorosulfonates do not yield the expected derivatives with the sulfonyl group attached to the phosphorus atom; such substances appear to be unstable and decompose in the course of the reaction.^{147,164} Secondary halides may give some by-products in the form of olefin derivatives through dehydrohalogenation.

An interesting form of the isomerization reaction exists in the series of tri-2-haloethyl phosphites, which undergo the reaction *per se*, with both the required structures being present in the same molecule, and yield the expected di-2-haloethyl 2-haloethanephosphonates by a unimolecular reaction. Variable amounts of a by-product, in the form of a polymeric alkane-phosphonate, are simultaneously formed as a result of polymolecular reactions.^{101,102,103} Although 2-haloethyl-dialkyl phosphites undergo the normal isomerization on heating, the diaryl analogs undergo what appears to be a bimolecular reaction that results in the formation of tetra-aryl ethanediphosphonates.¹⁰⁰ Tertiary esters in which two of the phosphorus valences are ester bound by a cyclic structure (from glycol esterification) also undergo the alkyl halide reaction. Derivatives of ethylene glycol usually undergo ring opening, whereas the derivatives of substituted glycol usually preserve the ring, and the

departing alkyl halide carries as its alkyl group the radical that was originally the third radical of the ester.⁴⁴ Trialkyl trithiophosphites do not undergo the above reaction in the usual sense. The alkyl halide attacks the divalent sulfur, and the subsequent cleavage results in the formation of a dialkyl dithiohalophosphite, $(RS)_2PX$, with the second product assuming the form $R'SR$.⁷³ Reactions of this type are described in Section VI of this chapter. Tertiary phosphites with less than three sulfur atoms react in a mixed manner, both the normal and the abnormal cleavages taking place.⁴⁰

Although trialkyl phosphites are oxidized rather slowly to the corresponding phosphates by the contact with atmospheric oxygen,⁹⁷ the thio analogs are attacked with considerable vigor. The oxidation products of the thio esters have not been identified under these conditions.⁴⁰ Oxidation of the trialkyl trithiophosphites by strong oxidizing agents yields phosphoric acid and alkanesulfonic acids.¹¹⁴

The interaction of halogens with tertiary phosphites forms the quasi-phosphonium compounds, $(RO)_3PX_2$, which are usually rather unstable. Although they can be isolated from the reaction mixtures of triaryl esters, they suffer spontaneous decomposition on heating (which takes place below room temperature in the series of the aliphatic esters). The products of the reaction are secondary halophosphates and the corresponding organic halides, $(RO)_2P(O)X$ and RX . Thus this reaction leads to the products obtainable by the direct halogenation of secondary phosphites. Since, as a rule, the tertiary esters are much more costly, it is obvious that the halophosphates are more economically made by the halogenation of the secondary esters. The reaction may be looked upon as a variant of the general Michaelis-Arbuzov reaction, in which the organic halide RX is replaced by the halogen molecule XX .^{4, 12, 33, 36, 81, 97, 102, 116, 117, 143, 155, 178} The reaction with cyclic esters, such as the glycol derivatives, is of interest. Chlorination of alkyl ethylene phosphites results in ring opening and yields alkyl 2-chloroethyl chlorophosphates; the similar treatment of ethylene chlorophosphite under similar conditions yields 2-chloroethyl dichlorophosphate.¹⁶²

The reaction of halogens with metal derivatives of secondary phosphites leads to the formation of a complex mixture. Although some dialkyl chlorophosphite is formed when chlorine is used,^{30, 31} the reaction normally yields the dialkyl phosphite radical, $(RO)_2PO$, which goes through a complex series of oxidation-reduction reactions that result in the formation of esters of hypophosphoric, pyrophosphorous, and pyrophosphoric acids, in a manner reminiscent of the behavior of the reaction mixtures of metal derivatives of secondary phosphites with some secondary organic halides.²⁹ For the description of the products see Chapter 12.

The reactions of the phosphites are customarily interpreted by the addition-cleavage mechanism, involving the quasi-phosphonium intermediates.^{15, 16} A few kinetic studies of the isomerization of tertiary esters have been made,^{168, 181} but the bulk of the interpretations has been made essentially on the basis of possible analogy.

Halophosphites and phosphites serve as useful intermediates for the synthesis of numerous organophosphorus compounds, a fact clearly seen from the wealth of reactions in which they participate. In addition to this transient utility, the tertiary esters have found fairly extensive use as antioxidants, particularly in the field of oil additives.

PHOSPHITES

HALOPHOSPHITES

BROMO DERIVATIVES

- Br-CH₂CH₂OPBr.** III. *b*₂ 79–80°, *d*₀²⁰ 2.3786, *n*_D²⁰ 1.6106.¹⁶¹
iso-BuOPBr₂. I. *b*₂₀ 85–7°, *d*₄¹⁷ 1.673.¹³²
MeCH(CF₃)OPBr₂. I. *b*. 156–7°, f.p. 48°.¹⁷³
PhOPBr₂. I. *b*₁₁ 130–2°.¹⁷⁰
(Br-CH₂CH₂O)₂PBr. III. *b*_{1.7} 114–5.5°, *d*₀²⁰ 2.1133, *d*₄²⁰ 2.1109, *n*_D²⁰ 1.5671. Not obtained in completely pure form.¹⁶¹
(PhO)₂PBr. I. *b*₁₁ 189–92°.¹⁷⁰

CHLORO DERIVATIVES

- MeOPCl₂.** I. *b*₇₅₈ 95–6°, *d*₄⁰ 1.4275, *d*₄²⁰ 1.3980, *n*_D²⁰ 1.47725.^{69, 110}
EtOPCl₂. I.¹²⁰ IV.⁶⁶ *b*. 117.5–9°, ²⁵ *b*. 117–8°, ¹³⁰ *d*₀⁰ 1.316, ¹²⁰ *d*₄⁰ 1.30526, ¹⁷⁸ *d*₄⁰ 1.3083, *d*₄²⁰ 1.2857, *d*₄¹¹⁷ 1.1831, ¹¹⁰ *n*_D²⁰ 1.47176, ¹¹⁰ *n*_D^{24.5} 1.46409.¹⁸²
ClCH₂CH₂OPCl₂. III. *b*. 172–5°, *b*₁₁ 59.5–60.5°, *d*₀²⁰ 1.4688, *d*₄²⁰ 1.4675, *n*_D²⁰ 1.5051.¹⁶¹
PrOPCl₂. I. *b*₇₅₅ 143–5°, ¹¹⁰ *b*₁₃ 40°, ⁴¹ *d*₄⁰ 1.2495, *d*₄²⁰ 1.2278, *d*₄¹⁴⁴ 1.1121, *n*_D²⁰ 1.46604.¹¹⁰
MeCH(CCl₃)OPCl₂. I. *b*₂₅ 130°, *b*₇₀ 140°, *b*₇₅₈ 223–4°, *d*₄²⁰ 1.5870.⁹⁸
CH₂:CH·CH₂OPCl₂. I. *b*_{742.5} 140.5°, ¹⁸³ *b*₇₅₈ 137°, ¹⁶² *d*₀⁰ 1.29003, *d*₀¹⁸ 1.2685.¹⁸³
BuOPCl₂. I.^{23, 81, 110} IV.⁸¹ *b*. 157°, ¹¹⁰ *b*₁₄ 56°, ⁸¹ *b*₁₈ 66–7°, ²³ *d*₄⁰ 1.1923, ¹¹⁰ *d*₄¹⁶ 1.1801, ⁸¹ *d*₄²⁰ 1.1657, ¹¹⁰ *n*_D²⁰ 1.46086.¹¹⁰
iso-BuOPCl₂. I. *b*. 154–6°, *d*₀⁰ 1.191.¹²⁰
iso-AmOPCl₂. I. *b*. 173°, ¹²⁰ *b*. 178°, ¹¹⁰ *d*⁰ 1.109, ¹²⁰ *d*₄⁰ 1.1563, *d*₄²⁰ 1.1364, *n*_D²⁰ 1.45566.¹¹⁰
***n*-C₆H₁₃OPCl₂.** I. *b*₂₄ 104°, *d*₀⁰ 1.1371, *n*_D^{16.5} 1.4669, ¹⁵⁷ *n*_D^{26.5} 1.4699.¹⁵⁶
***n*-C₇H₁₅OPCl₂.** I. *b*_{12.5} 107°, *d*₀⁰ 1.1138, *n*_D¹⁴ 1.4720.¹⁵⁶
***n*-C₈H₁₇OPCl₂.** I. *b*₁₂ 123–4°, *d*₀⁰ 1.0919, *n*_D²¹ 1.4682.¹⁵⁶
2-C₈H₁₇OPCl₂. I. *b*₁ 75–6°, ⁸³ *b*₂ 83–4°, ⁸² *b*₁₇ 118–9°, *d*₄¹⁸ 1.0749, *d*₄²⁶ 1.0683, *n*_D¹⁶ 1.4666, *n*_D¹⁹ 1.4669.⁸³
EtO₂C·CHMe·OPCl₂. I. *b*₁₅ 88°, *d*₄¹⁷ 1.2745, *d*₄³⁵ 1.2522, *n*_D¹⁹ 1.4654.⁸⁴
PhCH₂OPCl₂. I. *b*₁₁ 113–4°, *d*₀⁰ 1.3243, *n*_D^{19.4} 1.5584.^{156, 157} This product invariably explodes on distillation of the crude.
PhCH(CO₂Et)OPCl₂. I. *b*₂ 105–8°, *n*_D¹⁶ 1.5277.⁸³
PhOPCl₂. I.^{3, 143} IV.⁶⁹ *b*. 216° (dec.), *b*₁₁ 90°, *d*₁₈¹⁸ 1.348, *d*₄²⁰ 1.3543.^{3, 69, 143}
4-ClC₆H₄OPCl₂. I. *b*₁₂ 128–30°.¹⁷⁰
4-MeOC₆H₄OPCl₂. I. *b*₁₃ 130–1°, ¹¹ *b*₁₃ 135°, ⁷⁴ *n*_D²¹ 1.568.⁷⁴

- 2-MeC₆H₄OPCl₂**. I. b₁₁ 116°, ¹⁷⁰b₁₁ 106°. ⁵⁸
3-MeC₆H₄OPCl₂. I. b₁₂ 114°. ⁵⁸
4-MeC₆H₄OPCl₂. I. b₁₁ 118°. ¹⁷⁰
1-C₁₀H₇OPCl₂. I. b₁₅ 174-6°, d₀¹⁵ 1.0776. ¹¹¹
2-C₁₀H₇OPCl₂. I. b₁₅ 179-81°, d₀¹⁵ 1.0781. ¹¹¹
EtSPCl₂. I. ^{73, 121, 151}VI. ⁷³b. 171°, ¹⁵¹b₁₀ 53°, ⁷³b₁₀ 64°, ¹⁵¹b. 172-5°, d₀¹² 1.30. ¹²¹
PhSPCl₂. I. b. 213-7°, ⁶⁹b₁₀ 125°, d₁₅¹⁵ 1.2560. ¹²⁴
Cl₂POCH₂CH₂OPCl₂. I. b₂ 84-5°, d₂₀²⁰ 1.5689, d₄²⁰ 1.5655, n_D²⁰ 1.5280. ¹⁶²
m-C₆H₄(OPCl₂)₂. I. b₅₆ 240°, d₀¹⁸ 1.5696. ¹⁰⁹
p-C₆H₄(OPCl₂)₂. I. m. 65°, b₆₅ 200°. ¹⁰⁹

CHLOROPHOSPHITES WITH TWO DISCRETE RADICALS

- (MeO)(iso-BuO)PCl**. V. Obtained in crude form; b₁₇ 62-72°. ¹⁵⁶
(EtO)₂PCl. V. ^{30, 31}VII. ^{30, 31}b. 153-5°, b₃₀ 63-5°, d₀⁰ 1.0962, d₀²⁰ 1.0747, n_D²⁰ 1.4350. ^{30, 31}
(ClCH₂CH₂O)₂PCl. III. b_{4,5} 101-3°, d₀²⁰ 1.4019, d₄²⁰ 1.4007, n_D²⁰ 1.4950. ¹⁰¹
(EtO)(BuO)PCl. V. b₉ 72-5°. ¹⁵⁸
(EtO)(n-C₇H₁₅O)PCl. V. b₁₁ 122.5-4°, d₀⁰ 1.0249, n_D^{12.5} 1.4468, n_D²⁰ 1.4411. ¹⁵⁶
(PrO)₂PCl. V. ⁴¹II. ¹⁵⁶b₈ 65-5°, d₀⁰ 1.0626, n_D²⁰ 1.4420. ^{41, 156}
(CCl₃.CHMeO)₂PCl. I. b₂₅ 210°. ⁹³
(PrO)(BuO)PCl. V. b₉ 85-6°, d₀⁰ 1.1212, n_D²⁰ 1.4421. ¹⁵⁶
(BuO)₂PCl. IV. ⁸¹VI. ²³I. ⁸¹b₆ 91.5-2.5°, ²³b₁₂ 99-102°, ⁸¹d₀¹⁵ 1.014, n_D²⁰ 1.445. ²³
(n-C₈H₁₇O)₂PCl. V. Undistillable oil. ¹⁵⁸
(2-C₈H₁₇O)₂PCl. I. b₂ 135-40°, n_D²⁰ 1.4430. ⁸³
(EtO₂C.CHMeO)₂PCl. I. b₁₅ 155-60°. ⁸⁴
(EtS)₂PCl. II. VI. b₅ 84-5°, b₄ 83°, d₄²⁰ 1.2050, n_D²⁰ 1.5850. ⁷³
(PhO)₂PCl. I. ^{3, 143}IV. ⁶⁹b₁ 165-74°, ⁸⁹b₇₃₁ 295°, b₂₂₁ 265-70°, b₁₁ 172°, d₁₈¹⁸ 1.221. ^{3, 143}
(4-ClC₆H₄O)₂PCl. I. b₁₁ 225-7°. ¹⁷⁰
(2-MeOC₆H₄O)₂PCl. I. b₁₃ 235°, n_D²¹ 1.586. ⁷⁴
(2-MeC₆H₄O)₂PCl. I. b₁₁ 190°, ⁵⁸b₁₁ 195-6°. ¹⁷⁰
(3-MeC₆H₄O)₂PCl. I. b₁₁ 198°. ⁵⁸
(4-MeC₆H₄O)₂PCl. I. b₁₁ 206-8°. ¹⁷⁰

CHLOROPHOSPHITES WITH PHOSPHORUS IN A RING SYSTEM

- $\overbrace{\text{CH}_2\text{CH}_2\text{O} \cdot \text{PCl} \cdot \text{O}}^{\text{I.}^{162} \text{ II.}^{44}}$ b₁₀ 41.5°, ⁴⁴b₄₇ 66-8°, ¹⁶²d₀²⁰ 1.4172, ⁴⁴d₄²⁰ 1.4199, ²⁰d₂₀²⁰ 1.4229, ¹⁶²n_D²⁰ 1.4894, ¹⁶²n_D²⁰ 1.4915. ⁴⁴
 $\overbrace{\text{MeOCH}_2\text{CHCH}_2\text{O} \cdot \text{PCl} \cdot \text{O}}^{\text{II.}}$ b₉ 78.5-9.2°, d₀²⁰ 1.2984, n_D²⁰ 1.4722. ⁴⁴
 $\overbrace{\text{MeCHCH}_2\text{CH}_2\text{O} \cdot \text{PCl} \cdot \text{O}}^{\text{II.}}$ b₁₂ 65°, d₀²⁰ 1.2496, n_D²⁰ 1.4765. ⁴⁴
 $\overbrace{\text{CH}_2\text{CH}_2\text{CH}_2\text{CH}_2\text{O} \cdot \text{PCl} \cdot \text{O}}^{\text{II.}}$ b₈ 74-5.5°, d₀²⁰ 1.2858, n_D²⁰ 1.5010. ⁴⁴
 $\overbrace{\text{CH}_2\text{CH}_2\text{OCH}_2\text{CH}_2\text{O} \cdot \text{PCl} \cdot \text{O}}^{\text{II.}}$ b₁₅ 104-5°, d₀²⁰ 1.2693, n_D²⁰ 1.5165. ⁴⁴
1,2-C₆H₄O₂PCl. I. ^{3, 43, 48, 100}IV. ^{3, 10}Needles, m. 30°, ^{3, 42}b₁₀ 80°, ^{3, 42}b₁₀ 81-2°, b₆ 71-2°, ¹⁰⁰b₁₃ 86°, ⁴³b₁₆ 91°, ⁹b₆₅ 140°. ¹⁰⁹
(4-Me)-1,2-C₆H₄O₂PCl. I. b₁₁ 102°, m. 22-4°. ¹⁴
CIP(OCH₂CH₂O)₂PCl. Claimed as a reaction product of glycol with PCl₃ in dry ether. Undistillable oil. ⁶¹

MONOALKYL OR MONOARYL PHOSPHITES

- MeOPO₂H₂.** VIII.¹⁴⁶ IX.¹⁶⁶ Na salt, crystals, dec. 125° (from EtOH-Et₂O).¹⁴⁶ Ba salt, Ca salt monohydrate: unstable solids.¹⁶⁶ Free acid is an unstable oil.
- EtOPO₂H₂.** VIII.^{99, 137, 146, 146} IX.¹⁷⁹ Ba salt, hygroscopic solid (from EtOH).^{137, 179} Pb salt, sol. in EtOH.¹⁷⁹ Na salt, needles, m. 183° (from EtOH).^{99, 146, 146}
- ClCH₂CH₂OPO₂H₂.** IX. From poorly characterized reaction product of glycol with PCl₃. Isolated as barium salt (from H₂O).⁶¹
- HOCH₂CH₂OPO₂H₂.** X. Isolated as hygroscopic Ca and Ba salts.⁵⁹
- PrOPO₂H₂.** VIII. Ferric salt, solid, almost insoluble in water.¹³⁷ Sodium salt, needles, m. 195–6° (from EtOH).¹⁴⁶
- 1-Chloro-2(or 3)-hydroxypropyl 3(or 2)-phosphite.** X.⁶⁰ IX.⁶³ from poorly characterized reaction product of PCl₃ and glycerol prepared in ether solution. Isolated as poorly described barium and calcium salts.^{60, 63}
- 1(or 2)-glyceryl phosphite.** X. Isolated as water-soluble barium salt, which forms a trihydrate.^{59, 66, 116}
- iso-PrOPO₂H₂.** VIII. Barium salt, hygroscopic solid.¹³⁷ Sodium salt, needles, m. 132–3° (from EtOH-Et₂O).¹⁴⁶ Ferric salt, almost insoluble in water.¹³⁷
- (CF₃)CHMeOPO₂H₂.** IX. Isolated as barium salt, which is soluble 1:25 in water.¹⁷³
- BuOPO₂H₂.** VIII. Isolated as sodium salt: needles, m. 177.5–8.5° (from EtOH).¹⁴⁶
- iso-BuOPO₂H₂.** VIII. Isolated as poorly soluble ferric salt.¹³⁷
- iso-AmOPO₂H₂.** VIII.¹³⁷ IX.¹⁷⁹ Free ester is an unstable oil. Ferric salt is a poorly soluble solid.¹³⁷
- 2-C₈H₁₇OPO₂H₂.** VIII.⁸² IX.⁸² Oil, d_4^{15} 1.0210, d_4^{50} 0.9914, n_D^{16} 1.4400.⁸²
- Monoerythryl phosphite.** X. Obtained as a crude, poorly stable product, readily decomposed by cold water.⁶²
- 4-PhCH₂CH₂C₆H₄CH₂CH₂OPO₂H₂.** IX. The free ester is an oil that gives a crystalline sodium salt.¹⁶⁷
- PhCH(CO₂Et)OPO₂H₂.** IX. The free ester is an oil, insoluble in water.⁸²
- PhOCH₂CH(OPO₂H₂)CH₂OPh.** IX. Needles, m. 119–20° (from EtOAc). Ammonium salt is an oil. Calcium salt, crystals (from dil. EtOH).⁵⁶
- p-MeC₆H₄OCH₂CH(OPO₂H₂)CH₂OPh.** IX. Needles, m. 106–7° (from EtOAc). The ammonium salt is a water-soluble solid.⁵⁶
- o-MeC₆H₄OCH₂CH(OPO₂H₂)CH₂OC₆H₄Me-o.** IX. Prisms, m. 88–9° (from EtOAc). The calcium salt tetrahydrate forms needles (from dil. EtOH).⁵⁷
- m-MeC₆H₄OCH₂CH(OPO₂H₂)CH₂OC₆H₄Me-m.** IX. Needles, m. 85–7° (from CS₂-petroleum ether).⁵⁷
- p-MeC₆H₄OCH₂CH(OPO₂H₂)CH₂OC₆H₄Me-p.** IX. Crystals, m. 111–2° (from EtOAc).⁵⁶
- 4-Allyl-2-methoxyphenyl phosphite.** IX. Poorly soluble yellow powder; slightly soluble in hot water.¹⁴⁹
- 1-C₁₀H₇OPO₂H₂.** IX. Powder, m. 82°. Phenylhydrazine salt, m. 83°. ¹¹¹
- 2-C₁₀H₇OPO₂H₂.** IX. Crystals, m. 111°. Phenylhydrazine salt, m. 98–9°. ¹¹¹
- l-Menthyl phosphite.** IX. Crystals, m. 29°; decompose at 135°, with liberation of menthene. Ca, Ag, and Pb salts isolated. ¹³³
- Cholesteryl phosphite.** IX. Crystals, m. 158° (from benzene-petroleum ether). ⁷⁶
- 4-Hydroxy-tetrahydrofuryl-3-phosphite.** VIII, from tetrahydrofurylene-3,4-phosphite. Free ester is very unstable. Calcium salt monohydrate: needles (from EtOH-Me₂CO). ^{62, 65}
- H₂O₂POCH₂CH₂OPO₂H₂.** Combined VIII–IX on ClP(OCH₂CH₂O)₂Cl. Isolated as poorly characterized calcium salt. ⁶¹

1,2(or 1,3)-glyceryl diphosphite. VIII, on reaction product of PCl_3 with glycerol. Imperfectly characterized.⁶³

1,6(?) -Mannityl diphosphite. X. Isolated as hygroscopic Ca salt.⁶⁴

DIALKYL (OR DIARYL) PHOSPHITES

PHOSPHITES WITH TWO DISCRETE RADICALS

(MeO)₂POH. I.⁴⁸ II.¹³⁴ V.^{15,16} b_8 56.5°, ^{15,16} b_{10} 56-8°, ¹³⁴ b_{10} 55-5.5°, ⁴⁸ d_0^{20} 1.2184, ¹⁵ d_0^{20} 1.2004, ⁴⁸ d_0^{25} 1.1909, ^{15,16} n_D^{20} 1.4036.⁴⁸ Ag salt: crystals (from (EtOH)).¹⁵

(EtO)₂POH. I.^{26,27,48,116,145,163} II.¹³⁴ V.^{15,16} VIII.^{20,127} XI.¹⁵⁰ XII.¹²² XIII.¹⁷⁶ b_{8-10} 72°, ^{15,16} b_9 66-7°, ¹⁴⁵ b_9 72-3°, ¹⁷² b_{10} 71.0-1.5°, b_{11} 72°, b_{13} 77-7.5°, ³⁷ b_{14} 74-5°, ¹⁴⁵ b_{15} 80-5°, ¹²² b_{15} 75°, ⁴⁸ b_{20} 87°, ¹⁵ b_{20} 90°, ¹⁵⁰ b_{754} 187-8°, ¹⁵ b_{760} 187-8°, ¹⁶ d_0^{20} 1.0912, ^{15,16} d_4^{20} 1.0961, ³⁷ d_4^{20} 1.093, ¹⁶³ d_4^{20} 1.07368, ³⁶ d_0^{20} 1.0722, ^{15,16} d_0^{20} 1.0742, ⁴⁸ d_4^{188} 0.88955, ^{15,16} n_D^{20} 1.4080, ⁴⁸ n_D^{20} 1.40823, ³⁶ Sodium salt: needles, dec. 142-3°, if prepared from metallic sodium in ether.^{98,122,130} Obtained in solution when sodium ethoxide is used instead of metallic sodium.¹⁴⁵ Potassium salt: prepared from metallic potassium; crystals.³⁶ Silver salt: prepared from the ester or its sodium salt with silver nitrate.^{21,22,99,137} Colorless and stable when pure. Magnesium salt: from metallic magnesium; powder.¹³⁰ Cuprous salt: from cuprous oxide. Insoluble, colorless solid that is stable when pure.^{21,22,137}

(PrO)₂POH. I.⁴⁸ II.¹³⁴ V.^{15,16} VIII.²⁰ XIV.⁴¹ b_{8-10} 91°, ^{15,16} b_8 88-90°, ¹⁴⁶ b_{11} 91.5°, ⁴⁸ d_0^{20} 1.0366, ^{15,16} d_0^{20} 1.0207, ^{15,16} d_0^{20} 1.0184, ⁴⁸ n_D^{20} 1.4163, ¹⁴⁶ n_D^{20} 1.4172, ⁴⁸ n_D^{23} 1.4175.⁴¹ Sodium salt: solid.⁹⁸ Silver salt: essentially insoluble in water; prepared best from the sodium salt.^{21,98,137}

(ClCH₂)₂CHO)₂POH. I.⁷⁰ Unstable; b_2 180.⁷⁰

(CHI:CI·CH₂O)₂POH. Modified I (propargyl alcohol, iodine, and red phosphorus).⁹² Needles, m. 48-9° (from EtOH).⁹²

(iso-PrO)₂POH. I.^{48,116} V.^{15,16} $b_{8.5}$ 72-3°, ¹²⁶ b_8 69-71°, ¹⁴⁶ b_9 69.5°, ⁴⁸ b_{8-10} 69.5°, ^{15,16} b_{10} 76-7°, b_{17} 85-6°, ¹²⁶ b_{17} 82.5°, ¹¹⁶ d_0^{20} 1.0159, ¹⁸ d_0^{18} 0.9972, ^{15,16} d_0^{20} 0.9981, ⁴⁸ n_D^{20} 1.4008, ⁴⁸ n_D^{20} 1.4070.¹⁴⁶ Cuprous salt: colorless solid.¹³⁷ Silver salt: colorless crystalline solid; soluble in alkali.^{21,137}

(BuO)₂POH. I.⁴⁸ II.¹³⁴ b_8 116-7°, ¹⁴⁶ b_{10} 115°, ⁴⁸ b_{12} 124-5°, ¹³⁴ d_0^{20} 0.9888, ⁴⁸ d_4^{20} 0.99503, ¹³⁴ n_D^{20} 1.423, ¹⁴⁶ n_D^{20} 1.4240.⁴⁸ Sodium salt is very soluble in hydrocarbons.

(iso-BuO)₂POH. I.^{15,38,48,70} VIII.²⁰ b_9 105°, ⁴⁸ b_{11} 112.5°, ¹⁰⁶ b_{12} 105.6-6.5°, ⁷⁰ b_{14} 117.5°, ³⁸ b_{235-6} 235-6°, ³⁸ d_0^{20} 0.9942, d_4^{20} 0.9759, ^{30,35} d_0^{20} 0.9766, ⁴⁸ n_D^{20} 1.4200, ⁴⁸ d_0^{20} 0.9257(?).³⁸ Sodium salt: amorphous, stable to 200°.³⁵ Silver salt: colorless needles.^{21,137}

(MeEtCHO)₂POH. I.⁷⁸ b_{12} 101°.⁷⁸

(iso-AmO)₂POH. I.^{70,78,179} $b_{0.15}$ 75°, ⁷⁰ b_{10} 133°, ⁷⁸ $d_0^{19.5}$ 0.967.¹⁷⁹

(MeCH₂CHMe·CH₂O)₂POH. I.⁷⁸ b_{15} 142°.⁷⁸

(Et₂CHO)₂POH. I.⁷⁰ $b_{0.2}$ 72°.⁷⁰

(n-C₆H₁₃O)₂POH. I.⁴⁸ b_2 145-6°, d_0^{20} 0.9486, n_D^{20} 1.4325.⁴⁸

(Me₂CH·CH₂·CHMe·O)₂POH. I.⁷⁰ $b_{0.2}$ 81°.⁷⁰

(n-C₇H₁₅O)₂POH. I.⁴⁸ b_2 166-7°, d_0^{20} 0.9363, n_D^{20} 1.4382.⁴⁸

(n-C₈H₁₇O)₂POH. I.⁴⁸ b_3 190-1°, d_0^{20} 0.9286, n_D^{20} 1.4420.⁴⁸

(2-C₈H₁₇O)₂POH. I.^{82,84} II.⁸² IV.⁸² VIII.⁸² $b_{0.1}$ 116-8°, ⁸⁴ b_2 138-40°, d_4^{15} 0.9218, d_4^{15} 0.9176, d_4^{21} 0.9133, n_D^{18} 1.4375, n_D^{21} 1.4391(?), n_D^{23} 1.4370.⁸²

(EtO₂C·CHMe·O)₂POH. I (best in Et₂O solution).^{70,84} IX.⁸⁴ $b_{0.2}$ 135°, ⁷⁰ b_2 140-50°.⁸⁴ (crude).

(HO₂C·CHMe·O)₂POH. Modified I (reaction of PI_3 with conc. lactic acid, followed by treatment with water; the primary product appears to be an anhydride, $\text{C}_6\text{H}_9\text{O}_6\text{P}$, m. 120°).⁷⁹ Isolated as water-soluble calcium salt (octahydrate).⁷⁹

((2-MeC₆H₄OCH₂)₂CH·O)₂POH. IX.⁵⁷ Needles, m. 118–9° (from EtOAc).⁵⁷

((4-MeC₆H₄OCH₂)₂CH·O)₂POH. IX.⁵⁷ Plates, m. 81–2° (from EtOH).⁵⁷

(PhCH₂O)₂POH. (Dibenzyl phosphite). II.^{40, 50} XI.⁴⁰ As ordinarily prepared, the product melts at 0–5°; very pure samples m. 17°. *b*_{0.1} 165°, ⁴⁰*b*_{0.001} 110–20°. Satisfactory and safe distillation of this substance is possible only after treatment of the crude product with dry ammonia and must be conducted very rapidly in inert atmosphere in the presence of N-methylmorpholine.⁴⁰

(EtO₂C·CHPh·O)₂POH. I.⁸² Undistillable oil; *n*_D²⁰ 1.5200.⁸²

(Ph₂CH·O)₂POH. XI.⁴⁰ Crystals; decomp. 60°, m. 105° (on rapid heating).

On recrystallization decomposes with formation of dibenzhydryl ether; hence is used in crude form.⁴⁰

(PhO)₂POH. VIII.¹³⁸ *b*₂₅ 218–9°.¹³⁸

Dicholestanol phosphite. I.¹⁰⁶ m. 186°.¹⁰⁶

PHOSPHITES WITH PHOSPHORUS IN A RING SYSTEM

CICH₂CHCH₂O·POH·O. IX.⁴⁴ *b*₂ 144–5°, *n*_D²⁰ 1.4898.⁴⁴

EtOCH₂CHCH₂O·POH·O. IX.⁴⁴ *b*_{2.5} 127–9°, *n*_D²⁰ 1.4598.⁴⁴

Tetrahydrofurylene-3,4-phosphite. X.^{62, 65} Hygroscopic needles, m. 127°, subliming at 130–40°.^{62, 65}

HOP(OCH₂CH₂O)₂POH. IX.⁶¹ Isolated as calcium salt. The ester is rapidly hydrolyzed by water.⁶¹

TRIALKYL (OR -ARYL) PHOSPHITES

(MeO)₃P. II.^{39, 134} V.^{15, 16, 47} *b*₂₃ 22°, ⁴⁷*b*. 111–2°, ³⁰*b*₇₄₅ 110–1.5°, ¹³⁴*b*₇₆₀ 111–2°, ¹⁵*d*₀ 1.0790, ²⁰*d*₀ 1.0540,^{15, 16} ²⁰*d*₀ 1.0520,⁴⁷ *n*_D²⁰ 1.4095.⁴⁷ Salts with cuprous halides: A₂·CuI, m. 69–70°; A·CuCl, m. 190–2°; A·CuBr, m. 180–2°; A·CuI, m. 175–7°.^{15, 16} Adduct with AuCl, m. 100–1°.¹¹³ A·AuCl·2NH₃, m. 75–6°.¹¹²

(EtO)₃P. II.^{39, 47, 77, 116, 119} V.^{15, 16, 30, 97} XV.¹⁵¹ *b*₁₁ 48–9°, ⁹⁸*b*₁₂ 48.2°, ⁹⁸*b*₁₂ 49°, ⁴⁷*b*₁₄ 52°, ⁷⁷*b*₁₉ 55°, ¹¹⁹*b*₁₉ 57.5°, ⁷⁷*b*₇₄₀ 155–6°, ¹³⁴*b*₇₅₅ 154.5–5.5°, ¹¹⁹*b*₇₅₇ 157.9°, ³⁶*d*₀ 0.9777,^{15, 16} ⁰*d*₀ 1.0028,¹⁵¹ ¹⁷*d*₀ 0.9605,^{15, 16} ²⁰*d*₀ 0.9687,⁴⁷ ²⁰*d*₄ 0.96867,³⁶ ^{17.5}*n*_D 1.4140,⁷⁷ ²⁰*n*_D 1.41309,³⁶ ²⁰*n*_D 1.4134,³⁰ ²⁰*n*_D 1.4135.⁴⁷ Salts with CuCl, liquid; CuBr, m. 27–8°; CuI, m. 109–10°.^{15, 16} m. 111–2°.³⁰; AgCl, m. 4.5–5.5°; AgBr, m. 40–40.5°; AgI, m. 81–3°.³⁸

(EtO)₂POCH₂CH₂Cl. III (poor). II. *b*₅ 71–2°, ²⁰*d*₀ 1.1032, ²⁰*d*₄ 1.1025, ²⁰*n*_D 1.4391.¹⁰⁴

EtOP(OCH₂CH₂Cl)₂. II. *b*₆ 111–3°, ²¹*d*₀ 1.2292, ²¹*d*₄ 1.2283, ²⁰*n*_D 1.4617.¹⁰⁴

(ClCH₂CH₂O)₃P. II (poor).¹⁰⁴ III.¹⁰¹ *b*_{2.5} 112–5°, ²⁶*d*₀ 1.3453, ²⁶*d*₄ 1.3443, ²⁶*n*_D 1.4818.¹⁰¹

(BrCH₂CH₂O)₃P. III. Undistillable without isomerization.¹⁵¹

(Cl₃CCH₂O)₃P. I. *b*. 263°.⁷¹

(MeOCH₂CH₂O)₃P. II. *b*₅ 138.5–40°, ²⁰*d*₀ 1.0960, *n*_D²⁰ 1.4402.⁴⁷

(iso-BuO₂C·CH₂O)₃P. II. *b*₂ 185–215°.⁷²

P(OCH₂C(O)NBu₂)₃. II. Undistillable oil.⁷²

(PrO)₃P. II.^{39, 47, 134, 169} V.^{15, 16} XVI.¹³⁶ *b*_{8–10} 83°.^{15, 16} *b*₁₀ 82–4°, *b*₁₀ 83°, ⁴⁷*b*₁₂ 86–7°, ¹⁶⁹*b*₁₃ 89–9.5°, ³⁹*b*₂₄ 103°, ¹³⁴*b*. 206–7°, ²⁶*d*₀ 0.9705,^{15, 16} ²⁰*d*₀ 0.9522,⁴⁷ ^{21.5}*d*₀ 0.9503,^{15, 16} ²⁰*n*_D 1.4265. Salts: CuCl, liquid; CuBr, liquid; CuI, m. 64–5°.^{15, 16}

(NC·CMe₂·O)₃P. I. *b*₄ 153–4°, ¹²*d*₄ 1.082, ¹²*n*_D 1.4467.⁶⁷

(EtO₂C·CHMe·O)₃P. II. *b*₂ 150–5°, *n*_D¹⁰ 1.4382.⁶⁴

(iso-PrO)₃P. II.^{39, 77} V.^{15, 16} *b*_{8–10} 60–1°.^{15, 16} *b*_{12.5} 65–7°, ³⁹*b*₁₁ 63–4°, ²⁵*d*₀ 0.9361, ^{18.5}*d*₀ 0.9187,^{15, 16} Salts: CuCl, m. 112–4°; CuBr, m. 149–50°; CuI, m. 184–5°.^{15, 16}

- (BuO)₃P. II.^{89, 81, 134} V.³⁸ XVI.¹³⁶ b₈ 119.5–20°, b₁₀ 120°, ^{33, 136} b₁₂ 122°, ⁸¹ b₁₂ 122–3°, ¹³⁴ b₁₃ 125–6°, ³⁹ b₁₆ 125°, ⁸¹ b₁₈ 127–8°, ⁸¹ d₀⁰ 0.9309, ³³ d₄¹⁴ 0.9324, ⁸¹ d₀¹⁷ 0.9201, ³³ d₄²⁰ 0.92530,¹³⁴ d₄²⁰ 0.9259,⁸¹ d₄²³ 0.9247,⁸¹ n_D¹⁶ 1.4339, ⁸¹ n_D¹⁹ 1.4321.¹³⁶
- (iso-BuO)₃P. V^{16, 35} (poor). II.^{89, 47} b_{4,5} 100.5°, ^{16, 47} b₁₀ 135–6°, ²⁶ b₁₂ 107(?)°, ³⁹ b₂ 234–5°, ³⁵ d₀⁰ 0.919, ¹⁶ d₀⁰ 0.9184–0.9196, ³⁵ d₄⁰ 0.9193, ³⁵ d₀²⁰ 0.9040, ⁴⁷ d₄²⁰ 0.904, ¹⁶ d₄²⁰ 0.9036, ³⁵ d₀²⁰ 0.9052, ³⁵ CuI salt, m. 48°. ³⁵
- (iso-AmO)₃P. V. b. 270–5°, d₀¹⁵ 0.9005.^{97, 164}
- (2-C₈H₁₇O)₃P. II. b₂ 162–4°, d₄²² 0.8843, n_D²² 1.4449.⁸²
- PhOP(OCCH₂CH₂Cl)₂. III. b₂ 150–2°, d₀²⁰ 1.2854, d₄²⁰ 1.2845, n_D²⁰ 1.5270.¹⁰⁰
- (PhO)₂POCH₂CH₂Cl. III. b₁ 153–4°, b₂ 156–9°, d₀²⁰ 1.2347, d₄²⁰ 1.2336, n_D²⁰ 1.5584.¹⁰⁰
- (PhO)₂(PrO)P. II. XVI. b₂₄ 203–4°, d₄¹⁹ 1.1149.¹³⁶
- (PhO)₂(BuO)P. XVI. b₁₂ 198°, d₄²² 1.0917.¹³⁶
- (PhO)₃P. I.^{3, 47, 143} II.^{136, 169} b. 360°, ¹⁷ b₁ 209–10°, ⁸⁹ b₅ 200–1°, ¹⁶⁹ b₁₁ 220°, b₁₂ 228°, ⁴⁷ b₁₈ 235°, ⁴ d₁₈¹⁸ 1.184, d₀²⁰ 1.1844, ⁴⁷ m. 25°, ¹⁶⁹ m. 17–22°. ⁸⁹ Salts with cuprous halides: 2A·CuCl, m. 70°; 2A·CuBr, m. 73–4°; 2A·CuI, m. 73–5°; A·CuCl, m. 95–6°; A·CuBr, m. 90.5–1.5°; all crystallize from Et₂O.¹⁶ 2A·PtCl₂, m. 155°. ¹⁶⁰
- (PhO)₂(2-ClC₆H₄O)P. I. b₆ 238–46°, d₂₅²⁵ 1.159, n_D²⁵ 1.5932.¹³⁹
- (4-ClC₆H₄O)₃P. I. m. 49°, b₁₅ 290–7°. ¹²⁵
- (2-MeOC₆H₄O)₃P. I.⁷⁴ Older preparation by V⁵⁴ is faulty. m. 59°, b₁₃ 275–80°. ⁷⁴
- (4-O₂NC₆H₄O)₃P. I. Needles, m. 170–1° (from AcOH); decomposes above m.p.¹⁷⁰
- (*p*-tert-BuC₆H₄O)(PhO)₂P. I. b₇ 240–53°, d₀²⁵ 1.124, n_D²⁵ 1.5692.¹⁴⁰
- (*p*-tert-BuC₆H₄O)₂(PhO)P. I. b₇ 272–82°, d₀²⁵ 1.124, n_D²⁵ 1.5562.¹⁴¹
- (2-Me-5-iso-Pr-C₆H₃O)(2-ClC₆H₄O)₂P. I. b₁₀ 265–75°, n_D²⁵ 1.5762.¹⁴⁰
- (2-MeC₆H₄O)₃P. I. b₁₁ 238°, ⁵⁸ b₁₁ 248°. ¹⁷⁰
- (3-MeC₆H₄O)₃P. I. b₇ 235–8°, b₁₀ 240–3°, ¹²³ b₁₂ 248–50°. ⁵⁸
- (4-MeC₆H₄O)₃P. I. b₁₀ 250–5°, ¹²³ b₁₁ 285°. ¹⁷⁰
- Tri*p*seudocumyl phosphite. I. b₁₆ 270–4°, d₀¹⁷ 1.097.¹²³
- (4-tert-BuC₆H₄O)₃P. I. b₈ 288–94°, m. 75–6°. ¹⁴¹
- (4-Me₂C·CH₂·CM₂·C₆H₄O)₃P. I. b₁₀ 354–7°, n_D⁶⁰ 1.5205.¹⁴¹
- (2-PhC₆H₄O)(PhO)₂P. I. b₉ 280–90°, d₀²⁵ 1.184, n_D²⁵ 1.6152.¹⁴⁰
- (2-PhC₆H₄O)₂(PhO)P. I. b₉ 308–27°, d₀²⁵ 1.201, n_D²⁵ 1.6356.^{139, 140}
- (2-PhC₆H₄O)₃P. I. b₅ 336–40°, m. 95°. ¹⁴⁰
- Tri-*o*-cyclohexylphenyl phosphite. I. b₈ 324–9°, n_D⁶⁰ 1.5580.¹⁴⁰
- (1-C₁₀H₇O)₃P. I. m. 91° (from xylene).¹²
- (2-C₁₀H₇O)₃P. I. m. 94° (from xylene).¹²
- Tri-1-(2,4-dibromo)naphthyl phosphite. I. m. 289°; does not add bromine or chlorine.¹²
- Tri-2-(1,6-dibromo)naphthyl phosphite. I. m. 245°; does not add bromine or chlorine.¹²
- Tri-2-decahydronaphthyl phosphite. V. m. 75°. ⁹⁵
- Tri-1-anthryl phosphite. I. Decomp. 182–90°; does not add bromine or chlorine.¹²
- Tri-*l*-menthyl phosphite. II.^{131, 133} m. 44–5°. ^{131, 133}

PHOSPHITES WITH PHOSPHORUS IN A RING SYSTEM

- CH₂CH₂OP(OMe)O. II. b₂₈ 55–6°, ⁴⁴ b₃₅ 60–2°, ¹⁶³ d₀²⁰ 1.2159, ⁴⁴ d₂₀²⁰ 1.2067, ¹⁶³ d₄²⁰ 1.2044, ¹⁶³ n_D²⁰ 1.4448, ¹⁶³ n_D²⁰ 1.4460. ⁴⁴ CuI salt, m. 132–3°. ⁴⁴

$\text{CH}_2\text{CH}_2\text{OP}(\text{OEt})\text{O}$. II. b_{15} 50.5–51°, $b_{19.5}$ 61–2.5°, d_0^{20} 1.1317, d_4^{20} 1.1191, n_D^{20} 1.4395, n_D^{20} 1.4397.¹⁰² CuI salt, m. 90°. On treatment with water this ester gives what appears to be an open-chain ester, $(\text{EtO})(\text{HOCH}_2\text{CH}_2\text{O})\text{POH}$, which has n_D^{20} 1.4825, and b_{11} 142–3°.⁴⁴

$\text{CH}_2\text{CH}_2\text{OP}(\text{OCH}_2\text{CH}_2\text{Cl})\text{O}$. II. $b_{6.5}$ 78.5–9.5°, d_0^{20} 1.3206, n_D^{20} 1.4755.⁴⁴

$\text{CH}_2\text{CH}_2\text{OP}(\text{OBu})\text{O}$. II. $b_{8.5}$ 71–2°, d_0^{20} 1.0819, n_D^{20} 1.4470.⁴⁴

$\text{MeOCH}_2\text{CHCH}_2\text{OP}(\text{OMe})\text{O}$. II. b_9 77–8°, d_0^{20} 1.1798, n_D^{20} 1.4459.⁴⁴ On treatment with water, the ring system appears to be retained, yielding probably

$\text{MeOCH}_2\text{CHCH}_2\text{OP}(\text{OH})\text{O}$, b_{10} 156–8°, n_D^{20} 1.4719.⁴⁴

$\text{MeOCH}_2\text{CHCH}_2\text{OP}(\text{OEt})\text{O}$. II. b_{10} 84–5°, d_0^{20} 1.1415, n_D^{20} 1.4498.⁴⁴

$\text{EtOCH}_2\text{CHCH}_2\text{OP}(\text{OEt})\text{O}$. II. b_7 93–4°, d_0^{20} 1.0937, n_D^{20} 1.4401.⁴⁴

$\text{MeOCH}_2\text{CHCH}_2\text{OP}(\text{OBu})\text{O}$. II. b_9 107–7.5°, d_0^{20} 1.0713, n_D^{20} 1.4450.⁴⁴

$\text{ClCH}_2\text{CHCH}_2\text{OP}(\text{OBu})\text{O}$. II. b_8 108.5–10°, d_0^{20} 1.1629, n_D^{20} 1.4601.⁴⁴

$\text{MeCHCH}_2\text{CH}_2\text{OP}(\text{OMe})\text{O}$. II. b_{13} 62°, d_0^{20} 1.1092, n_D^{20} 1.4420.⁴⁴

$\text{MeCHCH}_2\text{CH}_2\text{OP}(\text{OEt})\text{O}$. II. b_8 63–4°, d_0^{20} 1.0696, n_D^{20} 1.4410.⁴⁴

$\text{CH}_2\text{CH}_2\text{CH}_2\text{CH}_2\text{OP}(\text{OMe})\text{O}$. II. $b_{4.5-5}$ 54–5°, d_0^{20} 1.1640, n_D^{20} 1.4642; CuI salt, m. 142–4°.⁴⁴

$\text{CH}_2\text{CH}_2\text{CH}_2\text{CH}_2\text{OP}(\text{OBu})\text{O}$. II. b_{9-10} 100–2°, d_0^{20} 1.0557, n_D^{20} 1.4540.⁴⁴

$\text{MeOCH}_2\text{CHCH}_2\text{OP}(\text{OPh})\text{O}$. II. b_7 145.5–46°, d_0^{20} 1.2130, n_D^{20} 1.4768.⁴⁴

$o\text{-C}_6\text{H}_4\text{O}_2\text{POMe}$. I.¹³ V.⁴² b_8 73°, b_{15} 76–7°, d_0^{15} 1.2568, n_D^{19} 1.5209.⁴² CuBr salt, m. 130–5°.⁴²

$o\text{-C}_6\text{H}_4\text{O}_2\text{POEt}$. I.¹³ V.⁴² b_{11} 83–4°, b_{11} 86°, d_0^9 1.2420, n_D^{17} 1.5085; CuBr salt, m. 142–5°.⁴²

$o\text{-C}_6\text{H}_4\text{O}_2\text{POCH}_2\text{CH}_2\text{Cl}$. III. $b_{2.5}$ 107–8°, d_0^{20} 1.3455, d_4^{20} 1.3444, n_D^{20} 1.5430; CuCl salt, m. 135–7°.¹⁰⁰

$o\text{-C}_6\text{H}_4\text{O}_2\text{POPPr}$. I.¹³ V.⁴² b_9 97°, b_{13} 100–2°, d_0^9 1.1120, d_0^{17} 1.1296, n_D^{17} 1.4841; CuI salt, m. 138°.⁴²

$o\text{-C}_6\text{H}_4\text{O}_2\text{POPPr-iso}$. V. b_3 73–4°, d_0^{17} 1.1171, n_D^{17} 1.4724; CuCl salt, m. 143°; CuI salt, m. 178–9° (with decomposition).⁴²

$o\text{-C}_6\text{H}_4\text{O}_2\text{POBu}$. I.¹³ V.⁴² b_8 116°, b_{12} 116–7°, d_0^9 1.1457, d_0^{17} 1.1255, n_D^{18} 1.5053; CuCl salt, sinters at 150°, m. 202°.⁴²

$o\text{-C}_6\text{H}_4\text{O}_2\text{POBu-iso}$. V.⁴² b_8 105°, d_0^9 1.1208, n_D^{15} 1.4950, d_0^{19} 1.0997; CuCl salt, sinters at 158°, m. 208–10°.⁴²

$o\text{-C}_6\text{H}_4\text{O}_2\text{POPh}$. I. b_{12} 150°.¹³

$o\text{-C}_6\text{H}_4\text{O}_2\text{POC}_6\text{H}_4\text{OMe-o}$. I.¹³ $b_{0.13}$ 137°, b_{13} 184°.¹³

$o\text{-C}_6\text{H}_4\text{O}_2\text{POC}_6\text{H}_4\text{OH-o}$. I.¹³ XVI.¹³ Original preparation⁸ is not satisfactory

for synthetic purpose. Use of dry ether in reaction of pyrocatechol with 1.5 moles of PCl_3 gives an 85% yield of this substance: n_D^{20} 1.12-3°, n_D^{117} 1.256,¹³ b_{12} 155°(?).⁸ Its acetyl derivative, said to be undistillable,⁸ actually $b_{0.02}$ 135°.¹³ This ester does not add sulfur,¹³ contrary to expectations.

$\alpha\text{-C}_6\text{H}_4\text{O}_2\text{POC}_6\text{H}_4\text{Me-}o$. I.¹³ b_{13} 159-60°.¹³

$\alpha\text{-C}_6\text{H}_4\text{O}_2\text{POC}_6\text{H}_4\text{Me-}m$. I.¹³ b_{11} 158-9°.¹³

$\alpha\text{-C}_6\text{H}_4\text{O}_2\text{POC}_6\text{H}_4\text{Me-}p$. I.¹³ b_{12} 164°, m . 25°.¹³

Tri- α -phenylene diphosphite. This product is usually considered to have the structure $\alpha\text{-C}_6\text{H}_4\text{O}_2\text{POC}_6\text{H}_4\text{OPO}_2\text{C}_6\text{H}_4$, and may be regarded, in part, as a cyclic derivative. I.^{8, 9, 10, 109} b_1 202-3°, b_{12} 240-5°, b_{14} 242-8°, n_D^{15} 1.353.⁸

THIOPHOSPHITES

$(\text{EtO})_2(\text{EtS})\text{P}$. V. b_{10} 75-7°, d_4^{20} 1.0213, n_D^{20} 1.4592.⁴⁰

$(\text{EtO})(\text{EtS})_2\text{P}$. V. b_{10} 108-11°, d_4^{20} 1.0681, n_D^{15} 1.5326.⁴⁰

$(\text{EtS})_3\text{P}$. I.¹²¹ (very poor). II.^{72, 114} b_{18} 140-3°, m . -32°, d_4^0 1.1883, d_4^{25} 1.1585, n_D^{25} 1.5689.¹¹⁴ MeI adduct, m . 191°;¹¹⁴ EtI adduct, m . 125-7°;⁷³ HgBr_2 salt, m . 184°; HgI_2 salt, m . 187°; AuCl_3 salt, m . 225°.¹¹⁴

$(\text{PrO})_2(\text{PrS})\text{P}$. V.⁴⁰ b_{12} 120-4°, d_4^{15} 1.0562, n_D^{17} 1.5241.⁴⁰

$(\text{PrO})(\text{EtS})_2\text{P}$. V.⁴⁰ b_{15} 128°, d_4^{15} 1.0487, n_D^{20} 1.5278.⁴⁰

$(\text{PrS})_3\text{P}$. II. b_{15} 164-9°, m . -65°, d_4^0 1.1277, d_4^{25} 1.0932; MeI adduct, m . 191°; HgBr_2 salt, m . 176°; HgI_2 salt, m . 182°; AuCl_3 salt, m . 208°;¹¹⁴ n_D^{25} 1.5350.¹¹⁴

$(\text{BuS})_3\text{P}$. II. b_{15} 174-80°, m . -100°, d_4^0 1.0773, d_4^{25} 1.0421, n_D^{25} 1.5305; MeI adduct, m . 198°; HgBr_2 salt, m . 148°; HgI_2 salt, m . 162°; AuCl_3 salt, m . 182°.¹¹⁴

$(\text{PhS})_3\text{P}$. I. Scales or needles, m . 76-7°.^{124, 174}

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Phosphates, Halophosphates, and Thio Analogs

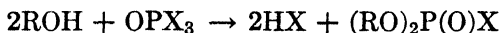
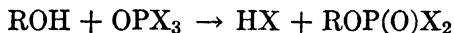
The substances considered in this chapter are the esters of phosphoric acid and the ester halides of phosphoric acid, as well as the analogs of these substances in which either part or all of the oxygen atoms are replaced by elements of the sulfur group.

Because of the large number of compounds in this family it was felt advisable to segregate the halogen derivatives into separate sections, both to discuss the methods of preparation and to list the properties of the known compounds.

METHODS OF PREPARATION OF HALOPHOSPHATES AND THEIR THIO ANALOGS

A. Reaction of hydroxy compounds with the halophosphoryl compounds

This is one of the simplest and most commonly used methods for the preparation of halophosphates. It consists essentially of the reaction of alcohols or phenols with substances like phosphorus oxyhalides (usually phosphorus oxychloride), or thiophosphoryl halides (usually thiophosphoryl chloride), in which the hydrogen of the hydroxyl and the halogen of the phosphorus compound are removed in the form of hydrogen halide. Roughly, the formation of either primary or the secondary derivatives depends upon the relative proportions of the reagents used.^{87, 241, 251, 442, 445, 483, 488}



With phosphorus oxychloride the reaction proceeds satisfactorily at room temperature or below room temperature when the hydroxy compound is a primary aliphatic alcohol. The successful outcome of the reaction depends to a considerable extent upon the removal of hydrogen halide; this is most satisfactorily accomplished by carrying out the reaction under somewhat reduced pressure with agitation,^{169, 251, 388} although bubbling of an inert gas, such as nitrogen or carbon dioxide

may be employed with somewhat less effectiveness.^{241, 488} The reaction may be restricted largely to the terms of the first equation by the employment of an excess of the oxyhalide. Although a stepwise reaction using two different alcohols may be visualized for the realization of the second equation, it has been shown that the second alcohol must have a higher alkyl radical than the first alcohol in order that any reaction may take place.²⁵¹ Secondary and tertiary alcohols, generally, do not react smoothly, and alkyl halide formation may be encountered; methyl-phenyl carbinol, for instance, yields such products exclusively.²⁴² (Schiff; Gerrard.)

The use of phosphorus oxyfluorodichloride in such reactions, run in the cold, results in preferential reaction of the two chlorine atoms and yields dialkyl fluorophosphates, $(RO)_2POF$.¹⁵⁵

Thiophosphoryl chloride reacts similarly with the primary alcohols and yields the halothionophosphates. However, its reactivity is lower and the reaction may be restricted to the formation of the primary derivatives, $ROP(S)Cl_2$, more readily than is the case for phosphorus oxychloride.^{400, 402} The lower alcohols react satisfactorily below room temperature,^{114, 185} whereas the higher ones (for example, butanol) may require heating.³⁵² The corresponding bromide has been used very rarely.⁴⁰²

Reactions with phenols require heating, usually at reflux point. Under these drastic conditions the restriction to monosubstitution is not very effective, even with excess of the halides, and the yields of monoaryl derivatives, as a rule, are decidedly short of theory.^{208, 265, 287, 357, 421, 434} The use of catalysts, such as magnesium chloride or oxide, has been recommended for the higher phenols.^{97, 434, 503}

The secondary halophosphates, $(RO)_2P(O)X$, may be prepared, in addition to the method indicated above, by the reaction of alcohols with the primary dihalophosphates, $ROP(O)X_2$. Although, on the face of it, the reaction shown in the second equation (see above) may be visualized as proceeding through the formation of the primary dihalophosphate, the behavior of the reaction mixtures suggests that the reactive material in the primary action may be a hydrogen-bonded adduct of the hydroxy compound with the phosphorus oxyhalide, or a quasi-phosphonium compound, $ROP(OH)X_3$, and that the dihalophosphate proper does not arise until the hydrogen halide is removed.³¹³ The reactions with the primary dihalophosphates generally need somewhat more drastic reaction conditions than are needed in the first reaction step. Mixed compounds, particularly the diaryl derivatives, can be prepared in this manner with moderate yields.^{97, 109, 368, 442} Aryl thionodichlorophosphates require high temperatures in such cases and give rather poor yields of the secondary derivatives.⁵³

The reactions with glycols have not been investigated satisfactorily, but dihydroxyphenols react very well. The meta and para derivatives react at both sites and form the tetrahalodiphosphates, whereas the ortho compounds readily form the cyclic phenylene halophosphates, that is, in effect secondary ester monohalides.⁴²⁶ Polyhydroxy phenols form resinous esters.¹⁰⁹

The halophosphates (or the thiono analogs) are isolated by distillation under reduced pressure. Only the lower alkyl derivatives have been successfully distilled, since the higher members decompose at the requisite temperatures. This is especially true of the secondary alkyl members, which must be distilled in high vacua, in any case, and only after all the hydrogen halide has been removed either by prolonged evacuation or by vacuum distillation of a volatile inert solvent.³⁸⁸ Because of the limited distillability, only a few of the alkyl derivatives have been isolated in the pure state. The aryl derivatives can be distilled satisfactorily.

Although many investigations of the nature of the reactions, described above, have been made, it must be admitted that the true and generally applicable formulation does not exist at this time.^{89, 115, 240, 241, 242, 268, 302, 303} It is very likely that the primary, and reactive, products are results of hydrogen bonding, which has been demonstrated for the phosphoryl group,⁴⁴ or their rearrangement products. It has been shown rather convincingly that the formation of alkyl halides, as by-products or total products, which takes place largely with the secondary alcohols, is not a result of decomposition of the halophosphates but rather the result of displacement reaction in the primary interaction.^{51, 242}

B. Halogenation of tertiary phosphites or secondary phosphites

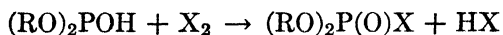
This reaction may be satisfactorily formulated as a special case of the Michaelis-Arbuzov reaction characteristic of trivalent phosphorus esters.



It has been applied very satisfactorily to a variety of aliphatic esters, both the tertiary phosphites having three discrete radicals and the esters with cyclic structure occupying two phosphorus valences. In the latter, the ring is cleaved and a haloalkyl group is formed in the final product, taking the place of the separation of alkyl halide shown in the basic equation above.⁴⁸⁶ The reaction is run in the cold, and any of the three principal halogens may be used.^{241, 292, 345, 488} The iodo derivatives, however, are too unstable to be actually isolated.^{177, 346} A logical extension of this reaction to the preparation of primary dihalophosphates from secondary monohalophosphites, $(\text{RO})_2\text{PX}$, has been explored with

moderate success; the applicability is limited by the poor methods available for the preparation of the starting materials.⁴⁸⁸

Although the reaction of tertiary phosphites cited above is satisfactory in many respects, it is rather costly because of the expensive methods needed for the synthesis of tertiary phosphites. This difficulty is obviated by a related reaction in which secondary phosphites are halogenated to yield secondary monohalophosphates.^{177, 314, 345, 441}



The reaction is conducted in the cold, and the products are isolated by vacuum distillation after thorough removal of the hydrogen halide by prolonged evacuation, preferably by codistillation with a volatile inert solvent.³¹⁴ Chlorine is usually used to form distillable products, since the bromo derivatives are essentially undistillable. Iodine does not react satisfactorily, and the previously described reaction of the tertiary esters must be used for the iodo derivatives.³⁴⁶ With proper care, substantially theoretical yields of secondary chlorophosphates are obtainable. Although chlorine per se is commonly used, sulfuryl chloride or thionyl chloride reacts similarly at somewhat higher temperatures (about 40°). The yields are somewhat poorer and the purity of the products somewhat less⁴¹ unless an inert solvent is used. This modification is satisfactory for such poorly stable substances as the dibenzyl derivative.⁴¹ (McCombie *et al.*; Kabachnik.)

C. Reaction of tertiary phosphates with phosphorus oxychloride

The reaction considered in this section may be regarded as a form of disproportionation. It has been applied with only moderate success to the higher alkyl esters. It is, however, rather effective with the lower esters at low temperatures (about 10° for triethyl phosphate) and moderately effective with selected aromatic esters, principally the cyclic compounds derived from catechol,^{24, 153, 154, 241, 311} on heating to about 150°.

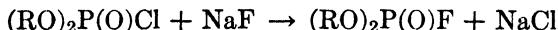


The reaction is far from quantitative, and drastic changes of reagent proportions give only moderate shifts of the ratios of the products.²⁴¹ There is no information about the relation of this reaction to the reaction observed between the same reagents (in the aliphatic series) at higher temperatures, a reaction leading to the polyphosphate esters (Chapter 12). In a related reaction a poor yield of dimethyl chlorothionophosphate was obtained from trimethyl thionophosphate and phosphorus pentachloride.¹⁵⁵

D. Exchange reaction of chlorophosphates

The chlorine atoms in chlorophosphates may be replaced readily by fluorine atoms. The resulting fluorophosphates have been made an interesting subject for study in recent years because of their physiological activity.

The chlorine-fluorine exchange is readily accomplished by heating the chlorophosphates with sodium fluoride in dry inert solvents; commonly benzene is used for this purpose.^{109, 314, 344, 441, 442}



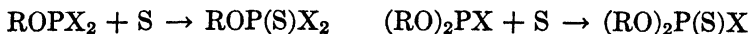
Although zinc fluoride and antimony trifluoride are unsuitable for such exchange reaction with the chlorophosphates because of complex formation,⁴⁴¹ the antimony reagent, especially when catalyzed by antimony pentahalides, is a satisfactory fluorinating agent for the thionochlorophosphates when used at moderate temperatures (below 50°);¹¹⁴ with dichloro derivatives it is possible to obtain either mono- or disubstitution.¹¹⁴

The exchange of chlorine for the cyano group, obtained on warming the chlorophosphates with potassium cyanide, is not a very satisfactory method for the preparation of the cyanophosphates, but the thiocyanate group may be introduced satisfactorily by using potassium thiocyanate.⁴⁴² The cyano group of secondary cyanophosphates may be exchanged for fluorine by the reaction with potassium bifluoride in hot benzene.¹⁰⁹ (Michaelis.)

Exchange reactions of the secondary chlorophosphates may be done in aqueous media at low temperatures; this cannot be done satisfactorily with the primary dichlorophosphates because of their greater hydrolyzability.¹⁰⁹

E. Addition of sulfur group elements to halophosphites

The halophosphites add the elements of the sulfur group to form the corresponding halothionophosphates. The addition requires conditions intermediate in intensity between the requirements of phosphorus trihalides and those of tertiary phosphites. (Michaelis.)

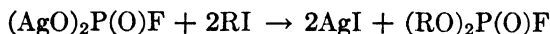


The alkyl dichlorophosphites react well even in boiling carbon disulfide⁴⁰⁶ whereas the aryl derivatives require much higher temperatures, usually above 150°. ^{15, 210, 455} The secondary chlorophosphites are similar.²⁰⁸ Selenium usually requires higher temperatures than sulfur, and some disproportionation of the phosphite may be encountered.⁴⁵⁵ The (S)-primary dichlorothiophosphites, RSPCl_2 , react similarly.^{359, 402}

Although elemental sulfur is commonly used, it is possible to use thiophosphoryl chloride as the source of sulfur in such reactions. This reagent donates its sulfur quite readily to phosphites and halophosphites on heating, and aryl halothionophosphates are satisfactorily prepared by such procedures at or near the boiling point.²⁴⁸

F. Reaction of salts of halophosphoric acids with alkyl halides

Reactions of this type are largely of historical interest only. Thus the first preparation of secondary fluorophosphates was accomplished by heating silver fluorophosphate with alkyl iodides in benzene.^{322, 441}

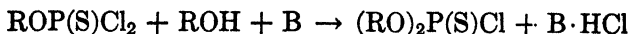
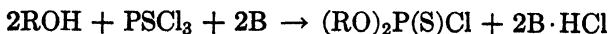
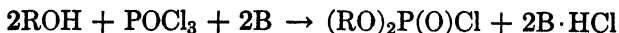


G. Reaction of hydroxy compounds, or thiols, with phosphorus oxydichlorofluoride

Although the chlorine atoms in POCl_2F are readily esterified by alcohols under mild conditions, the reaction with phenols or mercaptans does not proceed satisfactorily unless the theoretical amount of a tertiary base, usually pyridine or dimethylaniline, is present. The reaction is carried out in an inert solvent, and the resulting secondary fluorophosphate is isolated by distillation of the filtrate, after the removal of base hydrochloride.¹⁵⁵

H. Reaction of phosphorus oxyhalides, or halophosphates, with hydroxy compounds or thiols, in the presence of a base

The use of a theoretical amount of a tertiary organic base, usually pyridine, to take up the hydrogen halide in esterification of the halophosphoryl group is most commonly employed for the synthesis of the tertiary esters. However, a few halophosphates and halothionophosphates have been prepared by means of this reaction that employs a theoretical amount of the hydroxy compound, or thiol, and a theoretical amount of the base. The reactions are run in inert solvents, usually at or below room temperature, and the products are isolated after filtration.^{104, 212, 225, 352}



Experiments in which the chlorophosphates were not isolated as such, but were converted to amidophosphates, in situ, indicate that, although

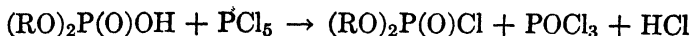
such reactions are governed to some extent by equations given above, products of higher and lower degrees of substitution also form. The maximum yield of the halides is obtained when two moles of the base are used per mole of phosphorus oxyhalide.⁴⁵ The chlorophosphates react with pyridine or pyridine hydrochloride on heating, yielding alkyl halides; the reaction is much more readily initiated in the primary derivatives than in the secondary derivatives.²⁴¹ (Milobendzki; Gerrard.)

I. Reaction of phosphorus pentachloride with hydroxy compounds

Although, generally speaking, hydroxy compounds react with phosphorus pentahalides either by chlorine-hydroxyl exchange or by the way of forming compounds of the types $(RO)PX_4$ or $(RO)_2PX_3$ (see Chapter 11), a few cases of halophosphate preparation have been reported. Usually the products are the secondary monochlorophosphates, which probably arise from the polyhalides, shown above, by secondary reactions with the unreacted hydroxy compounds.^{241, 243, 271, 303, 348} In general, secondary and tertiary alcohols give either no halophosphates or very small amounts, unless a tertiary base is present. The formation of alkyl halides or olefins in such cases appears to be the result of the primary reaction of the pentahalide.^{243, 268} Reactions of this type when applied to phenols require heating, which, in effect, decomposes the quasi-phosphonium compounds and produces substances of the halophosphate types.²²

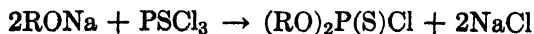
J. Conversion of phosphates or their salts into halophosphates

Reactions of this type have been used principally in the aromatic series. Thionyl chloride or phosphorus pentachloride have been used for the conversion of the alkali salts or the free phosphates, respectively, into the corresponding chlorophosphates.^{187, 300} The reactions are usually conducted with mild heating.⁵⁰⁶



K. Reaction of phosphoryl halides, or halophosphates, with alkali alkoxides or phenoxides

In the aliphatic series the reactions of this type are useful for the formation of secondary halothionophosphates (principally chloro), which are not formed satisfactorily by the direct reaction with the alcohols.



The relatively poor reactivity of the products permits the execution of such reactions in the presence of the respective alcohols; a simple form of usage employs two atomic equivalents of sodium dissolved in an excess of the alcohol. The products may be washed with water to remove salts.^{110, 216, 225} Products of higher and lower degrees of substitution may be formed.

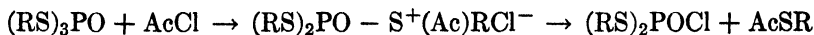
The aromatic series presents a wider scope for this reaction. The thiono derivatives, again, are chiefly used. Dry sodium phenoxide (or its substitution products) reacts with thiophosphoryl chloride on heating and generally yields the tertiary ester. The aryl dichlorothionophosphates, as a rule, do not react beyond the stage of disubstitution even on moderately strong heating, although at 200° the tertiary esters may be formed.^{51, 53, 340} However, thiophosphoryl chloride reacts well with phenols in the presence of aqueous sodium hydroxide and yields mixtures of primary and secondary halothionophosphates.^{51, 53, 375}



Since this reaction is also capable of formation of the tertiary esters, some of them may be found in the final mixture. Usually the best yields of the halothionophosphates are obtained in the cold, when 2 moles of phosphorus compound are permitted to react with 3 moles of the phenol in an excess of 10% sodium hydroxide with shaking.^{51, 53} The use of somewhat more concentrated alkali tends to increase the proportion of the secondary derivative.³⁷⁵ It is interesting to note that monoaryl dichlorothionophosphates do not react beyond the disubstitution stage even with 25 to 30% alkali either in the cold or on heating. This appears to be a sound argument for the rejection of the halothionophosphates as intermediates in the above reaction of thiophosphoryl chloride.⁵³ Mixed secondary derivatives may be synthesized by a stepwise procedure.³⁴⁰ Usually varying amounts of the thiophosphates, the hydrolytic products of the intermediates, are found in the alkaline solution and are readily separated from the insoluble halides.

L. Displacement reaction of tertiary thiophosphates

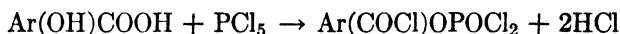
Although the final results of this reaction are analogous to those obtained by the reactions in Section C, the apparent mechanism of the present reaction is different. Tertiary trithiophosphates, $(\text{RS})_3\text{PO}$, react with acyl halides on heating and form secondary halodithiophosphates. Thus the ethyl derivative yields moderate amounts (about 40 to 50%) of (S,S)-diethyl chlorodithiophosphate on heating for 3 hours to 160° with acetyl chloride.¹⁰⁰



The reaction appears to be limited to the thioesters, that is, compounds with divalent, R-S-P, sulfur linkage, and probably proceeds via the addition as shown above. Continued action of an excess of the reagent can carry the product to further stages of degradation, $(\text{RS})\text{P}(\text{O})\text{Cl}_2$, and finally POCl_3 .

M. Reaction of phosphorus pentachloride with hydroxybenzoic acids

Phosphorus pentachloride reacts quite smoothly with hydroxybenzoic acids and forms the corresponding primary dichlorophosphates, which carry the chloroformyl groups at the site of the original carboxyls.^{10, 17, 179, 493-4} The reaction is best carried out by using a small excess of the pentachloride, and the mixture requires gentle warming for completion of the reaction.¹⁵ A small amount of phosphorus oxychloride is frequently beneficial.^{493, 494}



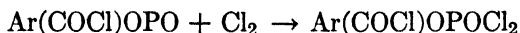
The reaction undoubtedly proceeds by the interaction of the carboxyls with the primary tetrahalides formed at the hydroxyls, a reaction common with the phosphorus polyhalides. Hydroxyaryl sulfonic acids, usually in the form of their sodium or potassium salts, undergo a similar reaction and form the chlorosulfonyl derivatives of primary dichlorophosphates, $\text{Ar}(\text{SO}_2\text{Cl})\text{OPOCl}_2$. Usually higher temperatures are required (about 100°), and mixtures of the pentachloride with oxychloride can be used at 150 to 180° with similar results,^{12, 21, 27, 514} although the higher temperatures usually tend to convert the chlorosulfonyl group into a chlorine substituent.²¹

If the chloroformylaryl dichlorophosphates are heated further with phosphorus pentachloride, a conversion to products containing five labile chlorine atoms takes place. These substances may be assigned two possible structures, $\text{Ar}(\text{COCl})\text{OPCl}_4$ or $\text{Ar}(\text{CCl}_3)\text{OPOCl}_2$. These substances are usually distillable liquids, which fact appears to favor the second formulation. The same products are obtained on heating the acyl chlorides of the aryl hydroxy acids with phosphorus pentachloride.^{13, 16, 18, 19} (Anschütz.)

N. Chlorination of metaphosphites

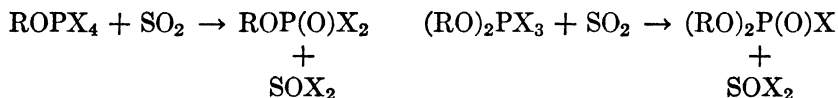
Reactions of this type have been used only with a specific group of substances, namely chloroformylaryl metaphosphites (see Chapter 12). The metaphosphite group adds two chlorine atoms and yields the corre-

sponding dichlorophosphates.^{13, 14, 16} A similar result is obtained when these esters are heated with one mole of phosphorus pentachloride.¹⁴ (Anschütz.)



O. Conversion of quasi-phosphonium polyhalides

Reactions involving the replacement of two halogen atoms by a semi-polar oxygen fall into this category. Usually the aryl derivatives are used because the aliphatic intermediates are poorly stable, and then the crude reaction products of the hydroxy compounds with phosphorus pentahalides (usually pentachloride) may be employed. Mild hydrolysis may be used in a few cases, but the most acceptable results are secured when sulfur dioxide is passed into the polyhalide.^{15, 195} Oxalic acid warmed with the trihalides may be used to prepare the secondary chlorophosphates.^{22, 24}



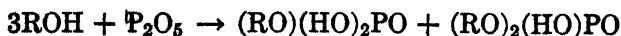
P. Oxidation of halothionophosphates

Usually thionophosphates may be converted to the phosphates by oxidation. A conversion of diaryl chlorothionophosphates to the corresponding halophosphates by means of nitric acid or hydrogen peroxide has been reported.²⁰⁶ The hydrolyzability of the products precludes the use of alkaline oxidizing agents, and under any conditions it is possible to use such procedures only when the products or the reactants can withstand the attendant hydrolytic tendencies.

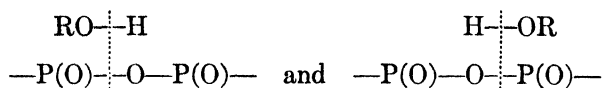
METHODS OF PREPARATION OF PHOSPHATES AND THIOPHOSPHATES

I. Reaction of hydroxy compounds with phosphorus pentoxide

This is one of the oldest and cheapest methods for the synthesis of mixtures of primary and secondary phosphates.^{3, 4, 90, 91, 107, 136, 146, 147, 151, 160, 259, 264, 339, 420, 473-4} In laboratory practice ether is the suspending agent for the solid pentoxide, in production the pentoxide-alcohol mixtures are used directly. When good agitation is available the solvent appears to be relatively unimportant. The usual representation of this reaction at the commonly used 3:1 ratio of the reagents is (Cavalier)



The over-all results may justify such formulations in a rough way only, because other products, namely phosphoric acid and very small amounts of tertiary esters, form concurrently. Examination of the actual conditions of such reactions, which in actual practice use considerably higher alcohol proportions than shown above, indicates that the true course of the reaction must be formulated otherwise. The pentoxide is not a monomeric molecule but has the structural unit of at least P_4O_{10} , which consists in essence of a closely knit network of phosphorus to oxygen to phosphorus bonds between the phosphoryl groups arranged approximately in a tetrahedron. The attack of an alcohol on such a structure proceeds by progressive cleavage of the anhydride bonds, which occurs essentially according to the laws of probability at any given instant and in each phosphorus to oxygen to phosphorus bond two "directions" of such cleavage can take place:



When such a process is followed through the destruction of all the anhydride linkages in the "pentoxide" unit, it is evident that the formation of primary and secondary esters is the predominant process. However, there is a minor probability that tertiary esters and phosphoric acid will be formed.

Such a picture is verified by the observations to the effect that considerably greater molar ratios of hydroxy compounds are needed to bring the solid pentoxide into solution than the ratio shown in the equation given above.⁴²⁰ Controlled experimentation is sadly lacking in the usual scientific literature on this reaction; one of the best recent pieces of work may be used as a point of departure for specific cases.¹⁶⁰

Since the primary and the secondary esters usually show decomposition symptoms at temperatures much above 100° , the reaction temperature is kept within such limits by suitable means. After completion of the actual dissolution of added pentoxide (usually four to five molar ratio of alcohol to the pentoxide is used), the mixture is quenched with water to hydrolyze any polyphosphate residues, and the individual primary and secondary esters are separated by fractional crystallization of suitable salts, when the radicals R are rather small. Barium salts are rather common, for the secondary esters yield barium salts that are much more water-soluble than those of the primary esters. Such procedures fail with the larger radicals, and the separations become extremely laborious if pure products are desired. In some cases use is made of the greater water solubility of the primary esters. The inorganic

phosphate is usually removed beforehand by magnesia mixture or lithium hydroxide, followed by removal of residual acid by magnesium chloride in dilute ammonium hydroxide.⁴⁷⁸ Pyridine has been claimed to have beneficial effects on the conduct of this reaction.⁴⁶¹

II. Reaction of hydroxy compounds with phosphoric acid, its acid salts, or polyphosphoric acids

The observations of esterification of alcohols by "sirupy" phosphoric acid are probably the true fountainheads in the development of the chemistry of organic derivatives of phosphorus.^{326, 335, 395, 396} In this crude form the reaction has little preparative significance. Modifications, such as heating the mixtures of hydroxy compounds with phosphoric acid to temperatures above 100° under reduced pressure, yield mixtures of esters that are similar to the product mixtures described in Section I.^{137, 140} As may be expected, polyhydroxy compounds yield complex mixtures, which may be resinous polymers. The complexity of the mixtures is reduced somewhat when mono- or disodium phosphate is used under such conditions. After treatment with water, mixtures of primary and secondary esters are obtained. For example, glycerol and monosodium phosphate, after several hours at 175° under reduced pressure, yield a mixture of monoglyceryl- and diglycerylphosphates. Alkaline treatment results in the formation of substantially pure monoglycerophosphate, which can be resolved into the individual isomers, 1- and 2-phosphates, by crystallization of the sodium salt of the 2-isomer from water.⁴⁷² The glycerophosphates also exhibit a shift between the 1- and the 2-esters, which may be utilized for the preparation of substantially pure 1-ester by boiling a dilute acid solution of the 2-ester.^{77, 78, 472} Although claims of formation of tertiary aromatic esters by such reactions have been made, it is difficult to visualize the realization of such a process.¹⁷³

The reaction of hydroxy compounds with linear polyphosphoric acids (or their salts) proceeds in the manner described for the phosphorus pentoxide reaction in Section I.¹⁶¹ Although claims have been made that such reactions result merely in esterification by the free acidic groups, all available information indicates that the reactions proceed not by such esterification,^{129, 299, 337} but by progressive cleavage of the phosphorus-oxygen-phosphorus anhydride links and give esters of acids of lower order of condensation and, in the end result, esters of phosphoric acid.^{4, 161, 165, 323, 469} Usually such reactions with pyrophosphoric acid are promoted by addition of sodium pyrophosphate.⁴³³ The reactions of this type, usually conducted with moderate heating, yield much higher ratios of the primary esters than the similar reactions with phosphorus

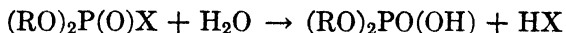
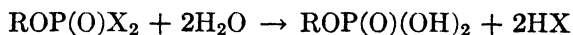
pentoxide, as is readily explained by the mechanism explained above. The mixtures obtained from such reactions, usually from thermally dehydrated phosphoric acid, are separated through the suitable metal salts, usually barium, or by ion-exchange resins.³⁴⁷

Solutions of phosphorus pentoxide in phosphoric acid, that is, partially hydrated phosphorus pentoxide mixtures, containing appreciable amounts of metaphosphoric acid, have been used for such reactions. The tendency to form esters of pyrophosphoric acid is fairly high in such cases, and a moderate excess of the hydroxy compound is advisable to carry the reaction to the expected mixture of primary and secondary esters, with high predominance of the former.^{165, 409} Such mixtures may be used for esterifications of hydroxy amino acids.³³¹

The precise mechanism of the cleavage of the anhydride links, shown in this Section and in Section I, is unknown. It is very likely, however, that the primary product is a hydrogen-bonded adduct to the highly polar phosphoryl groups, an adduct that may shift to a quasi-phosphonium compound, which then undergoes the actually observed cleavage.

III. Hydrolysis of halophosphates

The halophosphates are essentially acid halides; as such they are subject to hydrolysis to the corresponding free acids, at least in theory. The pure halophosphates may be hydrolyzed according to the equations



The lower alkyl dihalophosphates and the aryl derivatives may be hydrolyzed with moderate success by water treatment, at room temperature or somewhat above it. The secondary derivatives are usually fairly resistant to such mild hydrolysis and require higher temperatures, which favor partial hydrolysis of the ester links, especially in acid media. For this reason, the secondary halophosphates in general, as well as the primary dihalophosphates, are best converted to the salts of the corresponding acids with dilute aqueous alkali; the free acids may be obtained from these by acidification. Cyclic ester halides usually suffer ring opening upon hydrolytic treatment of any kind.⁴²⁶

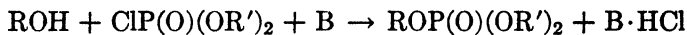
Often the individual halophosphates are not isolated, and the crude products of reactions between the hydroxy compounds and phosphorus oxychloride, with or without pyridine (Sections A and H in early part of the chapter), are hydrolyzed and the esters are separated in the usual manner.²¹⁹ Similarly, the reactions may be conducted by addition of

phosphorus oxychloride to the hydroxy compounds in aqueous solutions of inorganic bases, such as barium hydroxide or calcium hydroxide (less effective), or even dilute sodium hydroxide. In the aliphatic series reactions of this kind do not give very good yields and are usually "random" in character when polyhydroxy compounds are used.²¹⁴ Similar reactions in the aromatic series are in effect continuations of the preparations given in Section K.^{47, 51, 53} Such "one-step" methods probably do not involve the intermediate formation of true halophosphates.

Hydrolysis of halothionophosphates is complicated by transformation of the thiono group. Prolonged aqueous treatment results in the elimination of sulfur by oxidative hydrolytic processes. For this reason, alcoholic sodium, or potassium, hydroxide is used to form the thiophosphates, such as $(RO)_2POSK$.^{352, 402} Similar products result from "hydrolysis" of halophosphates by alcoholic solutions of potassium hydrosulfide.³⁵² The aromatic derivatives of this series, which are quite resistant to hydrolysis by water, usually require fairly drastic treatments.^{163, 172} Such products are more readily obtained by methods of Section K, from thiophosphoryl chloride.

IV. Reaction of chlorophosphates with blocked polyhydroxy compounds in the presence of tertiary bases

In contrast to the methods of the three preceding sections, which can yield random products with polyhydroxy compounds, as well as mixtures of products of varying degrees of esterification, the method considered in this section "pinpoints" the phosphorylation to a single location within the molecule. Secondary halophosphates react readily with derivatives of polyhydroxy compounds in which all but one hydroxy group are blocked from reaction. The result may be represented by the equation ¹¹⁹ (Brigl, Müller)



The blocking groups usually employed are those that can be removed with ease. Thus acetal blocking (frequently by means of acetone derivatives), acetylation, or tritylation is most commonly employed.^{41, 42, 57, 59} The acetal and the trityl groups may be removed by mild acidic hydrolysis; the acetyl block may be removed by catalytic hydrolysis with potassium methoxide. Compounds containing amino groups may have these blocked by the carbobenzoxy groups, which are often resistant to hydrogenative cleavage but are removable by acetic acid-phosphonium iodide treatment.⁴¹² Hydroxy acids may

require blocking of the acid groups by esterification before the phosphorylation can proceed satisfactorily.²³⁸

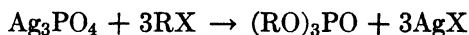
The radicals R' of the chlorophosphate are usually such as to be easily removable without cleavage of the phosphate link to radical R; phenyl or benzyl radicals qualify for this purpose quite well (see Section XVII).

Although pyridine has been the most commonly used base, the only study made to this date on the comparative effectiveness of tertiary bases in the reactions with halophosphates places pyridine at the bottom of the list.⁴¹ Quinaldine and 2,6-lutidine are most satisfactory; dimethylaniline is next. The particular reaction involved in this point is the gradual attack of the base on the halophosphate, resulting in the formation of a quaternary nitrogen ion, which takes in one of the R' radicals and, presumably, leaves the original halophosphate in the form of a metaphosphate.⁴¹ This decomposition is minimized by rapid reaction at moderately elevated temperature, instead of the traditional use of near-zero temperatures. More comparative studies of this kind are needed in order to delineate the best reaction conditions.

Attempts to use haloamidophosphates in such reactions have met with moderate success only because of the usual difficulty of complete removal of the amide groups.⁵⁰⁵

V. Reaction of alkyl halides with metal phosphates

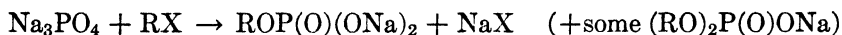
The classical form of this reaction yields tertiary phosphates by the reaction of silver phosphate with an excess of alkyl halide, usually the iodide, after a heating period of several hours.¹⁷⁰ (Clermont.)



Reactions of this type have found an application in the preparation of carbohydrate phosphates in recent years. It is of interest to note that silver phosphate in reaction with the alpha form of acetobromoglucose, followed by partial hydrolysis of the presumably tertiary ester, yields the alpha form of glucose-1-phosphate.⁴⁹⁵ Mixtures of the silver phosphate with phosphoric acid, yielding presumably a monosilver phosphate, yield essentially the primary esters, which can be isolated through the usual salts.⁵⁰⁸ Silver salts of secondary phosphates may be used to limit the reaction to primary esterification by the radical R. Silver dibenzyl phosphate has been used recently for such reactions because of the ease with which the benzyl groups are removed from the tertiary ester so obtained. This modification usually employs agitation of the warm reaction mixture in benzene.⁵⁰⁸ The reaction with acetobromoglucose, mentioned above, in this case yields the beta form of

the glucose phosphate; the structural conditions under which such inversions take place, in contrast to the reactions with silver phosphate, have not been explored adequately.⁴⁹⁵ Reactions of this type with the silver salts of thio- and dithiophosphates readily yield the corresponding tertiary (S)-alkyl esters.^{202, 400, 402, 432}

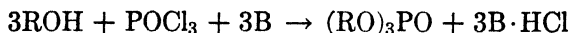
The less expensive sodium phosphates may be used in similar reactions, which, however, do not yield the tertiary esters but essentially the primary phosphates with moderate amounts of secondary esters. Trisodium phosphate in aqueous solution is generally used with the alkyl halides at temperatures above 60°, with progressively higher values for the larger alkyl groups.^{72, 147, 186} Disodium salts of primary phosphates may be used similarly to form the corresponding secondary phosphates.⁸⁴



Alkylation of trisodium phosphate, or the acid sodium phosphates, by dialkyl sulfates has been used for the synthesis of the primary esters (accompanied by some secondary esters), but the results have not been such as to supersede the alkyl halide reactions.⁷³

VI. Reaction of hydroxy compounds with phosphorus oxychloride, or thiophosphoryl chloride, in the presence of tertiary bases

This reaction is really an extension of the reactions given in Section H. Three equivalents of a hydroxy compound per one mole of phosphorus oxychloride, or thiophosphoryl chloride, in the presence of three equivalents of a tertiary base (pyridine, dialkylanilines, or quinoline have been usually employed) agitated in a suitable inert solvent give the best laboratory preparation of tertiary phosphates of all categories; thiono phosphates, when thiophosphoryl chloride is used.



The base hydrochloride may be filtered off or washed out by quenching the mixture with dilute acids.¹⁹⁸ The choice of the base should be made according to the data given in Section IV.⁴¹

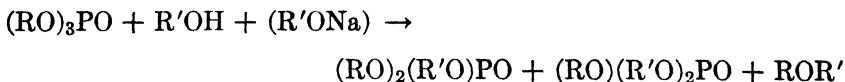
Use of lower ratios of the hydroxy compounds may be a source of the products of lower extent of esterification, and a number of primary esters have been made by such reactions after quenching the cold reaction mixture with ice-cold dilute mineral acids, followed by isolation of the esters in the form of suitable salts, usually calcium or barium.²¹⁹ It may be noted that glycol yields 2-chloroethyl phosphate by this method. The precise point in the process at which the exchange takes place has not been established.^{220, 409}

VII. Reaction of phosphorus oxychloride with blocked polyhydroxy compounds in the presence of tertiary base

The reactions in this section are in all respects identical with those given in the preceding section, except that the hydroxy compound used is a polyhydroxy derivative in which the "extra" hydroxyls are blocked by groups enumerated in Section IV. Thus the attack of the phosphorylating agent is limited to but one point in the molecule, although the extent of phosphorylation is not controllable to the extent afforded by methods of Section IV. The removal of the blocks was discussed earlier. (Fischer.)

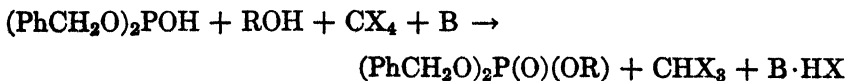
VIII. Exchange esterification of tertiary phosphates

Very little information is available about this reaction. Tertiary alkyl phosphates may be transesterified by heating with alcohols having a higher radical than that present in the ester. The reaction proceeds fairly readily in the presence of sodium alkoxide and results in the formation of mono- and diexchange products. The yields of individuals are rather poor, and mixtures are always formed. The trialkyl phosphate behaves like a normal alkylation agent, and the detached group forms ethers with the alkoxide ions.⁴³⁸ A partial representation follows.



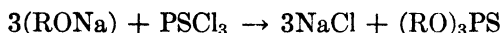
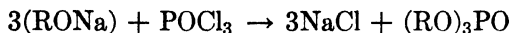
IX. Reaction of alcohols with secondary phosphites in the presence of aliphatic polyhalides and tertiary bases

Although mixtures of dialkyl phosphites with polyhalides, such as carbon tetrachloride and carbon bromotrichloride, behave like secondary halophosphates in their reactions with primary and secondary amines, such mixtures are ordinarily ineffective for esterification of hydroxy compounds. Dibenzyl phosphite does react in the sense of esterification under properly selected conditions only; it is possible that such condition selection may widen the scope of the reaction. The necessary conditions include use of the most efficient base (2,6-lutidine) and a reactive polyhalide (of the number of these investigated, carbon bromotrichloride is best, but carbon tetrachloride or tetrabromide may be used).^{41, 43} The reaction is run at room temperature and is a very mild procedure, but the yields of the alkyl dibenzyl phosphates are at best modest. (Todd *et al.*)



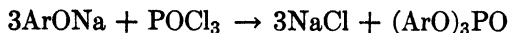
X. Reaction of phosphoryl halides, or the thiono analogs, with sodium alkoxides or sodium phenoxides

The reactions included in this section are continuations of the basic reactions cited in Section K. Generally speaking, the use of 1 mole of phosphorus oxychloride, or thiophosphoryl chloride, per 3 moles of the sodium derivative of a hydroxy compound yields the corresponding tertiary esters.



The general conditions used are similar to those given in Section K. The sodium derivatives used in anhydrous state in inert solvents give satisfactory yields of the trialkylphosphates or thionophosphates.^{53, 336, 402} If solutions of the alkoxides in alcohols are used, some primary and secondary esters are usually found among the by-products.⁴⁰² Sodium mercaptides react similarly and yield the corresponding (S)-trialkyl trithiophosphates or (S)-trialkyl tetrathiophosphates, respectively.^{53, 155, 402}

Mixed derivatives may be obtained by using the appropriate halophosphates or halothionophosphates. The reactivity of these, however, is much lower and conditions must be more drastic. This is especially true of the aryl derivatives, particularly in the thiono series. The diaryl halothionophosphates do not react with phenols in alkaline solutions, even on warming, although very strong heating in the dry state does form a moderate amount of the tertiary esters. The aromatic tertiary derivatives can be obtained in satisfactory yields, however, by the Schotten-Baumann method (see Section K), using 10% sodium hydroxide.⁴⁷



The corresponding thionophosphates are similarly formed from thiophosphoryl chloride on warming with 25 to 30% sodium hydroxide.^{15, 51, 53} The triaryl tetrathiophosphates require but 10% alkali,⁵³ and thiophenols react similarly.⁵² By-products in the form of primary and secondary esters always form.^{47, 53, 402} The poor reactivity of secondary halothionophosphates mentioned earlier leads to unduly drastic conditions for their further esterification by sodium salts of phenols in inert solvents, such as refluxing in chlorobenzene for one or two days;^{110, 225} such reactions proceed quite readily with the dialkyl derivatives in aqueous or alcoholic media.²²⁵

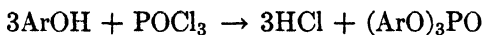
These results indicate that the halophosphates, especially those of the thiono series, are probably not the intermediates in the reactions

that employ phosphorus oxychloride or thiophosphoryl chloride, especially under the Schotten-Baumann conditions.

An excess of sodium alkoxide in contact with phosphorus pentahalide yields the tertiary phosphate, $(RO)_3PO$.¹³⁶ Reactions of this type may be used in the aromatic series. In most instances, however, the use of the less expensive oxychloride leads to the same results.

XI. Reaction of phosphorus oxychloride, or thiophosphoryl chloride, with an excess of a hydroxy compound or a thiol

When an excess of a phenol is heated with phosphorus oxychloride, generally satisfactory yields of triaryl phosphates are obtained.



Such reactions are, in a sense, a continuation of the reactions cited in Section A. The reactions are facilitated by magnesium chloride,⁹⁵ ultra-violet irradiation, or traces of iodine.⁴³⁷ Usually alkaline wash to remove partial esters is advisable prior to the distillation of the tertiary esters.¹¹⁸ Removal of hydrogen chloride by inert gas blowing or by a recycled inert solvent is also beneficial.⁴⁴⁸ Thiophosphoryl chloride reacts very unsatisfactorily, even on prolonged reflux. However, addition of a catalytic amount of phosphorus trichloride brings the formation of triaryl thionophosphates to essentially quantitative yields in short time. Apparently triarylphosphite formed instantaneously accepts sulfur from the thiophosphoryl chloride.²⁴⁸

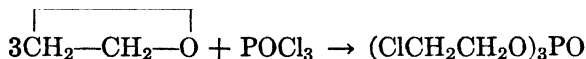
Thiols react poorly under such conditions, and only low yields of the tertiary esters are formed.⁴⁶¹

The formation of tertiary esters in the aliphatic series requires a set of conditions quite different from the requirements of the aryl derivatives. High temperatures cannot be used, for distillation of such mixtures gives but minute amounts of the tertiary esters.⁸⁹ The primary requisites may be listed as follows. A substantial excess of the alcohol over the theoretical amount must be used, in conjunction with low, or at most moderate, temperatures under conditions of rapid removal of hydrogen chloride (in effect this is done by the tertiary bases in Section VI ^{198, 241, 279} in similar conditions). Hydrogen halide may be removed by prolonged evacuation with stirring or by blowing with inert gas,⁴⁶⁸ or by washing the crude reaction mixture with cold aqueous alkaline solutions.^{201, 275, 276, 471} Finally, the use of dry ammonia as the final "clean-up" agent has been suggested.²⁰¹ The imposition of such conditions, taken in toto, indicates that the final product of such interactions is probably largely a compound of a quaternary type, possibly a quasi-phosphonium compound, which is decomposed to the tertiary phosphate

during the final "purification" steps that are essential before a distillable product may be secured. The use of metal derivatives of alcohols, given in Section X, obviously does not require such "clean-up" procedures, but is considerably less economical.^{174, 175, 213}

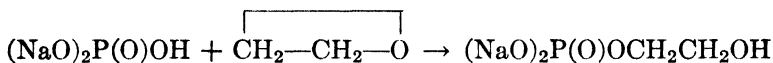
XII. Reactions of olefin oxides and imines

Olefin oxides, such as ethylene oxide, react with phosphorus oxychloride on warming in the presence of suitable catalysts, such as iron filings^{277, 280} or aluminum chloride,¹⁸² and form the corresponding tertiary haloalkyl phosphates, which form as a result of ring opening.



Lower ratios of the oxides presumably yield primary and secondary halophosphates.

Reaction of acidic hydroxyls in phosphoric acid or its partial esters similarly yields hydroxyalkyl phosphates. In like manner, disodium phosphate opens the ring of olefin oxides and gives primary hydroxyalkyl phosphates.^{42, 69}



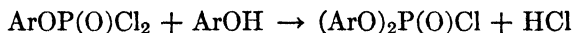
The general reaction of cyclic olefin oxides, imines, or sulfides with phosphoric acid, which yields tertiary esters by ring opening that may be augmented by further condensation at the active terminations of the alkyl groups, has been claimed in patent literature.² Specifically, ethylene imine, used in deficient amount, readily forms monoaminoethyl phosphate on being warmed with sirupy phosphoric acid.¹⁸⁴

XIIA. Reaction of olefins with phosphoric acid. Although patent literature contains claims of formation of acid esters of phosphoric acid by addition of phosphoric acid to various olefins, at elevated temperatures and pressures in the presence of sulfuric acid, no individual compounds have been reported.²⁸³ Similar addition to metaphosphoric acid has been described.¹⁹¹ It has been suggested that the use of phosphoric acid is most satisfactory in the presence of cuprous oxide or silver sulfate catalysts at 140°.³⁷⁴ The results of such reactions need considerable elucidation before discussion.

XIII. Reaction of halophosphates with hydroxy compounds

As was mentioned earlier, the aryl halophosphates react satisfactorily with phenols at elevated temperatures and afford a rather efficient preparation of tertiary aryl esters, symmetric or mixed, depending on

the phenols used. The reactions are run essentially at the reflux point, and metallic catalysts mentioned earlier are useful.



In the aliphatic series, such reactions do not proceed at all well beyond the first equation given above. The second step, performed either directly or indirectly, requires the use of tertiary bases for satisfactory yields at the necessarily moderate temperatures. Under such conditions the experimental requirements are identical to those given in Section IV.

XIV. Oxidation of phosphites

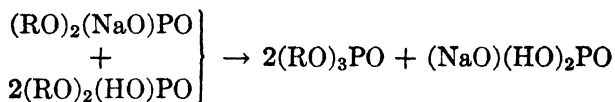
Although direct oxidation of tertiary phosphites to the corresponding phosphates by such methods as heating in a current of air⁶¹² or by treatment with air-sulfur trioxide mixtures¹²⁶ has been reported, these preparations have little practical significance in view of the costly preparation of tertiary alkyl phosphites, in the aliphatic series, and the generally adequate direct preparations in the aromatic series.

The formation of primary or secondary phosphates by oxidation of the corresponding phosphites by "wet" oxidation methods is not satisfactory because of extensive hydrolysis of the starting materials.

Indirect oxidation of the tertiary esters by adding a molar equivalent of halogen (usually bromine), followed by hydrolytic or alcoholic treatment, is fairly satisfactory in the laboratory (see Chapter 8).

XV. Thermal decomposition of salts of alkyl phosphates

Disproportionation of lead diethyl phosphate into triethyl phosphate and lead monoethyl phosphate at 200° was reported many years ago.⁴⁷⁴ Similar disproportionations of barium salts are known.³²³ However, the reaction approaches practical significance with the sodium salts,^{393, 498} which decompose similarly at approximately 300°.



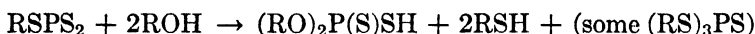
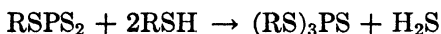
XVI. Reactions of alkyl metaphosphates and thio analogs

Alkyl metaphosphates, $(\text{ROPO}_2)_n$, can be hydrolyzed to substantially pure primary phosphates, ROP(O)(OH)_2 , with admixtures of some secondary and, to a lesser degree, tertiary esters from disproportiona-

tion.^{323, 409} Alcohylic reactions conducted at somewhat elevated temperatures give mixtures of secondary and tertiary esters.^{323, 409} These become quite complex if the radicals of the alcohol and of the ester are different because extensive disproportionation takes place. The reaction may be visualized also as progressive phosphorus-oxygen-phosphorus bond cleavage in the metaphosphate aggregate (see Section I, also Chapter 12).

The formation of tertiary alkyl esters from crude alkyl metaphosphates, which probably goes through a stage of oxonium-type adducts, has been reported. Thus acetals can supply the requisite alkoxy radicals to convert the alkyl metaphosphates to the corresponding tertiary esters at temperatures of about 100°. ²⁷² Similarly, ethers can form the tertiary esters on heating with phosphorus pentoxide to similar temperatures; ²⁷³ in this case the alkyl metaphosphate is formed in situ (see Chapter 12). The oxonium intermediates appear to be reasonable from the available data on the thermochemistry of ethers in similar systems.⁴⁶³

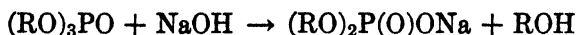
Alkyl trithiometaphosphates, RSPS₂ or its aggregates, have been studied only briefly, but their reactions have been shown to be similar to the oxygen analogs, with the added complication of oxidative changes on contact with air. The derivatives studied (thiophenol and benzyl mercaptan) react with phenols or thiophenols as shown below.⁴³⁵



The acid esters are best isolated in the form of nickel salts.⁴³⁵

XVII. Removal of ester groups

XVIIA. Partial hydrolysis of esters. Tertiary phosphates can be hydrolyzed readily to the secondary esters. Especially in the aliphatic series, such reactions can be used for synthetic purposes when alkaline solutions are used. The alkyl derivatives are attacked even at room temperature, provided that the radicals are moderately large; increased radical size rapidly increases hydrolysis resistance.^{85, 150, 192, 409} Acidic hydrolysis is more difficult to control, and generally progressive degradation products, down to phosphoric acid, are formed.



Hydrolysis of tertiary thiono esters by aqueous media usually results in the loss of sulfur, especially if the process is of long duration, and the

(O)-type esters result. For preservation of the sulfur content alcoholic alkali hydrosulfides may be used, which yield the monothiophosphates in the form of the metal salts; ^{202,402} alcoholic potassium hydroxide also works similarly. ³⁸²

Tertiary phosphates containing two phenyl or benzyl groups may be hydrolyzed usually by mild treatment with dilute mineral acids at moderately elevated temperatures. Selective removal of one group may thus be performed, but general conditions must be found experimentally in each case. ⁵⁷

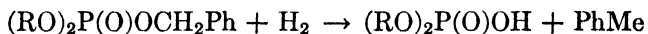
Studies of the detailed mechanism by hydrolysis in O^{18} -rich water, which appears to be the most logical method for such investigations, show that in alkaline hydrolysis the usually expected displacement of the OR group occurs. In acidic or "water" hydrolyses a rupture of the O-R link takes place, at least in the first step. ¹¹² This indicates the formation of either oxonium or quasi-phosphonium intermediates, which on the usual cleavage of such substances yield the partial esters.

Usually the secondary esters are quite stable to alkaline hydrolysis, and further attack occurs only under fairly drastic conditions. In acids the hydrolysis proceeds rather rapidly, but generally at a slower pace than shown in the hydrolysis of the tertiary esters. ^{84, 85, 150, 409}

Primary aliphatic esters are rather stable to alkaline hydrolysis but are attacked by acidic media on heating. ^{77, 78, 83, 183, 186, 408, 472} The nature of the radicals is important. Alkyl groups usually show a double-inflection-rate curve, with essentially no hydrolysis at pH 8, a pronounced maximum about pH 4-5, a minimum at about pH 1, and a rapid rise in more acidic solutions. ¹⁸⁶ Monoglycol phosphate shows a sharp maximum at pH 3-5, with the rest of the curve being similar to the above; ¹⁸⁶ glycerophosphate hydrolysis shows a shifted maximum at pH 3; ⁷⁹ simple carbohydrate phosphates, like diose phosphate, glucose-2-phosphate, and fructofuranose-6-phosphate, show a minimum at pH 2-3, a maximum at pH 7, and a continued rise of hydrolysis rate in acidities beyond pH 1. ²²⁹ The hydrolytic treatment of glycerophosphates, in addition to the hydrolysis, also involves the transposition of the phospho group. This is a reversible reaction with an equilibrium point at 87% 1-phosphate, attained readily by heating crude glycerophosphates in dilute mineral acids. This phenomenon is useful for the isolation of pure 1-isomer. ^{77, 78, 472} A similar transposition occurs in xylose. ³²⁹

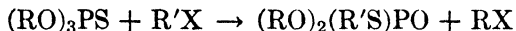
XVIIB. Hydrogenolysis of phenyl or benzyl esters. The phenyl or the benzyl groups can generally be removed from the corresponding phosphates by catalytic hydrogenation. This mild method of de-esterification is commonly used in connection with the reactions of a

type indicated in Section IV (and others) to prepare derivatives of polyfunctional compounds. The hydrogenolysis, however, does not operate smoothly in all cases, and no general conclusions on the occasions of failures may be made at this time. The most extensive study of conditions most favorable to success indicates the use of ethanol or dioxane for the solvent, preferably in the presence of a little water and a trace of acid (bases retard the action). Although platinum, nickel, or palladium catalysts may be used, palladium oxide appears to be most effective. Shaking the solution with a preliminary amount of the catalyst is useful in removing catalyst poisons.⁴¹



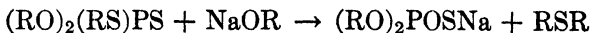
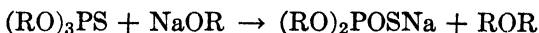
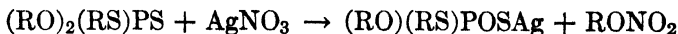
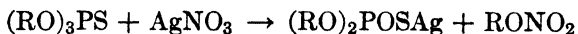
XVIII. Transformations of thiono esters

Tertiary esters containing the thiono group undergo isomerization and transformation reactions which approximate the isomerizations of the phosphites. The common feature of these reactions is the transfer of the semipolar sulfur of the thiono group to divalent state, with assumption of the semipolar state by oxygen, which comes from the OR groups of the original ester.^{182, 402} (Pishchimuka.)



Such transformations become isomerizations if $\text{R}=\text{R}'$. The mechanism probably involves preliminary addition to the semipolar sulfur.⁴⁰² Esters that in addition to the thiono group possess one (or more) thioalkyl group react similarly, but by-products caused by the attack of the alkyl halides (usually iodides) upon the P-S-R link with its consequent cleavage, reduce the yields of the normally expected esters.⁴⁰² These reactions are usually performed in sealed tubes at 100° or above.

Somewhat similar results are obtained when the thiono esters are allowed to react with a variety of inorganic salts or sodium alkoxides. The following salts are effective: HgCl_2 , HgI_2 , FeCl_3 , FeBr_3 , PtCl_4 , AgNO_3 , AgNO_2 , and AuCl_3 . Mercurous and ferrous salts do not react so far as is known, nor do the dihalides of nickel, cobalt, lead, or platinum.⁴⁰² The reaction is believed to proceed via addition of the cation to the semipolar sulfur atom, which is followed by the displacement of the "sulfonium" structure by a quasi-phosphonium structure and thermal decomposition of the latter structure. The cation remains bound to the thiophosphoryl group. These reactions, which take place either spontaneously or on mild heating, may be represented as shown below.^{400, 402}



The selenium compounds behave similarly.⁴⁰²

XIX. Controlled hydrolysis of tertiary pyrophosphates

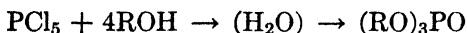
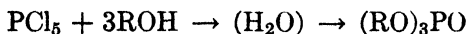
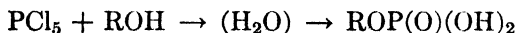
Tetra-alkyl pyrophosphates may be conveniently hydrolyzed to two equivalents of dialkyl phosphates by water at moderately elevated temperatures. The products obtained are almost pure, and much of the troublesome separation of the primary and secondary esters (see Sections I and II) is eliminated.⁴⁶⁶ (Toy.)



XX. Reaction of hydroxy compounds with phosphorus pentachloride

The reaction of phosphorus pentahalides with alcohols leads largely to the formation of alkyl halides, which is followed by the normal action of the resulting phosphorus oxyhalides. The effect is most pronounced in secondary and tertiary alcohols.^{243, 268, 399} The secondary reaction, as expected, is facilitated by the presence of pyridine and results in the formation of a spectrum of esters (see Section VI).

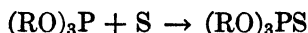
Phenols react with the formation of quasi-phosphonium halides (see Chapter 11), which are usually not isolated as such, but the crude mixtures are treated with water or dilute aqueous alkali to form the corresponding esters. As a rule, a spectrum of esters is formed in practice, either from disproportionation, or from non-homogeneity of the intermediate products.^{49, 449, 453}



Thiols do not appear to form esters with phosphorus pentahalides, but suffer oxidation to the disulfides.⁴⁹

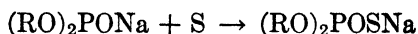
XXI. Addition of elements of the sulfur group to phosphites

Tertiary phosphites add sulfur (and related elements) quite readily on warming in inert solvents (usually carbon disulfide or the hydrocarbons) and form tertiary thionophosphates, selenophosphates, etc.



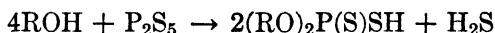
It is conceivable that intermediate products of "dimeric" structures may form if less than theoretical amounts of the element are used.³⁶⁹ Thiophosphoryl chloride may be used instead of sulfur as the sulfur donor.²⁴⁸

Secondary phosphites do not add sulfur, but their alkali metal salts enter the addition reaction spontaneously and form secondary thiophosphates in the form of the corresponding salts. The reactions are performed in anhydrous solvents. Selenium behaves similarly.²³²



XXII. Reaction of phosphorus pentasulfide with hydroxy compounds or thiols

The reaction of hydroxy compounds with phosphorus pentasulfide probably takes place by a similar mechanism of the pentoxide reaction. There is very little reliable information about the products obtained when ratio of an alcohol or phenol to the pentasulfide differs from four to one, at which predominant formation of secondary dithiophosphates takes place.^{132, 349, 402, 439, 481}



The free acid esters are fairly readily attacked by oxidative-hydrolytic action of aqueous reagents on exposure to the atmosphere; immediate conversion to metal salts is advisable for this reason.⁴⁰² The warming of the reaction mixtures necessary for completion of the interaction should be moderate, because temperatures much above 100° cause a secondary reaction—loss of hydrogen sulfide and formation of the thio analogs of the pyrophosphates.¹³²

The reaction given above is not the only one that takes place, since some free sulfur, alkyl sulfides, and unidentified products may be found in the residual liquors.^{402, 403} Evolution of mercaptans that occurs at higher temperatures is also a result of some unknown secondary reactions.^{365, 403, 481} Probably the entire course of the reaction should be regarded as a gradual cleavage of the phosphorus-sulfur-phosphorus bonds of the "pentasulfide" structural unit.

The reaction of thiols, in three to one molar ratio, has been reported to yield tertiary tetrathiophosphates; the reaction probably involves the formation of the trithiometaphosphates (see Section XVI and Chapter 12).⁴³⁹

The reported formation of esters of the types $(\text{RS})_2\text{P(O)OH}$ and $(\text{RS})(\text{RO})\text{P(O)OH}$ from cholesterol and phosphorus pentasulfide should

be reinvestigated because of the divergence of the results from normal. Both the large size of the radical and the extensive treatment of the products during purification may have been sources of erroneous conclusions.⁴⁸¹

In conclusion, the formation of acidic products from olefins and phosphorus pentasulfide, reported in patents,³⁰¹ should be mentioned. Such materials are probably not homogeneous, and, if the action consists of olefin addition across the structural units of the pentasulfide, both thiophosphate esters and thiophosphonic acids may be expected to form.

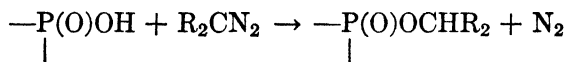
XXIII. Oxidation of thiophosphates

As has been mentioned in the previous sections, extensive hydrolytic treatment of compounds with the thiono group or a sulfhydryl group, such as exist in the thiophosphates, results in progressive loss of sulfur as hydrogen sulfide, with replacement by oxygen.

A more clean-cut reaction is the oxidation of tertiary thionophosphates by strong oxidizing agents, such as nitric acid, to the corresponding tertiary phosphates.⁴⁰² As a rule, such reactions have little practical significance.

XXIV. Reaction of diazoalkanes with the acid phosphates

A very clean and mild esterification of the acid groups in phosphoric acid or its primary or secondary esters is accomplished by the conventional reaction of diazoalkanes.⁴¹



GENERAL CHARACTERISTICS

The halophosphates and their thio analogs are essentially acid halides. Although, generally speaking, they are of interest merely as intermediates, the recent discovery of profound physiological action of the fluorophosphates, especially the secondary esters, opened new avenues of research interests in this series.³⁴⁴ In addition to the hydrolytic reactions and esterifications cited in the previous sections, these substances form amides with basic nitrogen derivatives (see Chapter 10). The Würtz reaction of secondary halophosphates, or thiono analogs, is said to yield dimeric substances,²⁰⁷ which are probably dimerized radicals similar to the hypophosphates (see Chapter 12). The precise structure of the chlorophosphate derived from ethanolamine has not been established; it may involve an amidophosphate structure.¹⁰⁶

Determination of hydrogen bonding in tertiary phosphates and phosphoryl halides shows a rapid rise of the "additive" factor in the oxygen of the phosphoryl group upon esterification.^{44, 351} The halophosphates are probably intermediate in this respect. In this way the entire series, from phosphoryl halides to tertiary esters, may be expected to have a progressive increase of additive affinity at the oxygen atom that provides the driving force for such reactions as the formation of polyphosphates from the esters and the halophosphate derivatives (see Chapter 12).³¹³

The tertiary esters, which may be regarded as essentially neutral derivatives of phosphorus, show the semipolar bonding of the oxygen or the sulfur in the P(O) or P(S) groups, in parachor and molecular refractivity measurements, rather than the double bond character.^{36, 37, 476} The tertiary phosphates alkylate phenols to phenol ethers,¹⁹⁸ and alcohols to the corresponding symmetric or mixed ethers,⁴⁶⁵ whereas primary aromatic amines are readily alkylated to the N-dialkyl amines.^{108, 462} The tertiary phosphates are quite stable to oxidation, and purification of crude esters by aqueous permanganate has been suggested as a method for obviating the customary vacuum distillation.¹⁶⁸ Although amidation of triethyl phosphate and of triethyl thionophosphate to diethyl amidophosphate by the action of ammonia under anhydrous conditions has been reported,⁴⁰² such reactions of the esters do not appear to be general, and the particular example cited deserves re-examination.

Primary and secondary phosphates are strong acids, di- and monobasic, respectively. Determination of the acid strengths in the aliphatic series shows a progressive rise upon alkylation, in comparison with phosphoric acid, a rise that is regressive with the size of the alkyl group, with a dialkyl ester being a stronger acid than the corresponding monoalkyl ester.³²⁰ Indication of hydrogen bonding of the ethyl ester, in its apparent formation of such a bond at the second carbon atom, appears from a decreased proton affinity. The hydroxy derivatives vary in their acid strengths. The variation is caused by hydrogen bonding either to the hydroxyl oxygens (acid weakening) or to the phosphoryl group (acid strengthening), as well as by steric factors.³²⁰ It is interesting to note that the alkaline hydrolysis of the primary esters begins to be noticeable at a pH that corresponds to the point of complete neutralization; the point of hydrolytic maximum observed at pH 4 (or thereabout) corresponds to the half-neutralization state.¹⁸⁶

The progressive fall of the acid strength with increased size of the radicals undoubtedly is responsible for the formulation of a number of complex derivatives, such as the cholesteryl, in the form of a "pyrophosphate" by Wagner-Jauregg.^{212, 481, 482, 505} In such cases the substances may be regarded as dimeric or trimeric phosphate ions, asso-

ciated in ring-like structures by hydrogen bonding. As such, these esters form acid salts with the alkali metals that also appear to have similar associated ring structures.^{215, 274, 433, 481}

Although metal salts of the thiophosphates have been reported in two forms in a few instances, forms presumably involving metal to sulfur or metal to oxygen bonding,⁴⁰² such results have not been duplicated elsewhere. It seems probable that no definite structure assignment is possible in such cases, but it is logical to assume a preponderance of bonding to sulfur, in view of its ready displacement from the semi-polar state by oxygen in the various transformation reactions of thionophosphates. The reactions of such salts with cyanogen chloride yield sulfur-bonded esters of the pyrophosphate types,³⁴³ and reactions with alkyl or acyl halides give the corresponding sulfur-bonded derivatives.^{343, 364} Halogenation or electrolysis yields dimers of the secondary thiophosphate (or dithiophosphate) radicals, which behave, at least in the case of the thiophosphates, in a manner analogous to true halogens.^{232, 342} These substances were named "phosphatogens" in provisional nomenclature by Foss,²³² and their redox potentials were determined in a series of dialkyl derivatives. These, generally liquid, neutral substances are best prepared by the halogenation method. They are only moderately stable in aqueous media and exhibit typical radical or polar cleavage reactions of the unit $(RO)_2POS \cdot SOP(OR)_2$.²³² Such compounds have been obtained in much earlier experiments of the Autenrieth school, but their nature was not made clear at that time. The selenium analogs are quite similar, but are less stable.

Although perphosphates, similar to the phosphatogens, may be visualized, only the patent literature appears to be the source of information about such compounds, allegedly formed on treatment of the higher alkyl phosphates with hydrogen peroxide.¹³⁰

Oxidative transformations of the organic substituents of the aliphatic phosphate esters have been used for synthesis of a variety of products. Drastic oxidation of glycerophosphates by alkaline hydrogen peroxide leads to dephosphorylation and extensive cleavage;³⁸⁶ at room temperature the carbonyl and aldehyde derivatives are attacked.¹⁸¹ Nitric-chromic acid mixture does not attack alkyl phosphates at room temperature, but the hydroxy derivatives are converted to the corresponding carboxy derivatives or to products of intermediate stages.¹⁸⁰ Periodic acid oxidation of glycerophosphates has been made the basis of a quantitative analytical procedure. The 2-phosphate is not attacked at room temperature; the 1-isomer is oxidized to the diose-phosphate.^{226, 231}

The usual organic transformations may be performed with the phosphate esters, provided that their hydrolytic tendency is kept in view.

The direct substitutions of the aromatic types have been studied rather incompletely. Usually, the phenyl derivatives react primarily at the para positions, but minor amounts of the ortho isomers may be detected.

The interesting subject of the naturally occurring phospholipids is beyond the scope of this volume. The reader is referred to reviews of the subject in periodic literature⁴⁹⁹ and to the usual literature of modern biochemistry, such as the *Annual Reviews*.

The family of the phosphates and the halophosphates, which includes substances of extremely diversified physical and chemical properties, is well represented in both the actual and the potential practical application fields. The neutral esters, especially, have been finding wider and wider application as solvents and plasticizers. The high order of compatibility of these esters is unquestionably related to the very pronounced tendency of the oxygen of the PO group to enter hydrogen-bonded structures, a tendency mentioned in the opening statements of this section. The earliest applications covered the more readily obtainable triaryl esters, but the recently improved procedures for the trialkyl derivatives have been responsible for the increasing use of these and of the mixed alkyl aryl esters. In addition to the plasticizing action the esters confer a degree of flame retardation to the formulations. This action is most pronounced in halogenated compounds, but is definite even in the unsubstituted derivatives. Obviously, the effect declines with a significant increase of the purely organic part of the molecule. The acid esters have been mentioned rather often in the patent literature in connection with surface active agents. The effectiveness of these substances, per se, is quite high and is parallel to that of the sulfur analogs, but the insolubility of the heavy metal salts in water reduces the potential uses in practice in comparison with the sulfates or the sulfonates. However, secondary esters of dithiophosphoric acid, that is, compounds of the type $(\text{RO})_2\text{PS}_2\text{H}$, particularly in the form of their salts, have been used rather extensively as ore flotation agents and lubricating oil additives.

Although the halophosphates are generally useful merely as intermediates for the synthesis of diversified derivatives, an exception must be made for the fluorophosphates, particularly the compounds $(\text{RO})_2\text{POF}$. These substances possess powerful anticholinesterase action, which varies with the substituent radicals and is extremely well shown by the lower alkyl esters. The high order of toxicity of these substances and the powerful myotic action produced by them at low atmospheric concentrations made them of considerable importance in the development of new warfare agents for both sides in the Second World War. Discussion of the results is not possible at this time.

However, generally speaking, the biological effects are similar to those produced by tetra-alkyl pyrophosphates (see Chapter 12).

This strong biological activity suggested the application of the fluorophosphates for insect control, and it appears correct to state that the fluorophosphates were the first phosphorus-containing substances successfully tried as insecticides by I.G. Farbenindustrie A.G. in the years just preceding the war. This development evidently stirred the investigations into other types of phosphorus derivatives having similar biological effects. The derivatives of pyrophosphoric acid, which resulted largely from this work, are discussed elsewhere in this book. However, a number of neutral tertiary esters of phosphoric acid were found to have even more toxic properties, and it is to the research organization of the I.G. Farbenindustrie that the credit must be given for the discovery of insecticidal activity of thiophosphates and phosphates that lack the fluorine and the pyro structure. One of these esters, diethyl *p*-nitrophenyl thionophosphate, has been rather widely used in this country in recent years for insect control as a result of the original disclosures of the German investigators. In closing this brief statement on biological activity of some members of this family, it is necessary to add that the high order of activity against insects is coupled with more general toxicity, as may be expected, and that these substances, when exposed, should be handled with appropriate care. A complete study of the toxicity of these substances on repeated exposures to low concentrations is yet to be made because of their relative novelty on the market.

HALOPHOSPHATES AND HALOTHIOPHOSPHATES

I. COMPOUNDS WITH ESTER BOND TO ALIPHATIC CARBON

A. ALKYL DIHALOPHOSPHATES. $\text{ROP}(\text{O})\text{X}_2$

EtOP(O)F₂. D. Liquid, b. 85–6°. ⁴⁴²

MeOP(O)Cl₂. C. Liquid, b₁₅ 62–4°. ¹⁵³

EtOP(O)Cl₂. A. ^{357, 442, 453, 488} B. ⁴⁸⁸ C. ¹⁵⁴ Liquid, b. 167°, ^{357, 488} b₁₉ 63°, ⁴⁴² b₁₀ 64–5°, ¹⁹ d₄ 1.353. ⁴⁸³

ClCH₂CH₂OP(O)Cl₂. A. ^{183, 251, 410, 429} B. ⁴⁸⁶ Liquid, b₁₅ 108–10°, ⁴²⁹ b₁₂ 103°, ^{183, 410} b₅ 81.5°, b₂ 71.5°, ⁴³⁶ b_{0.8} 96°, ²⁵¹ d₄ ²⁰ 1.5527, ²⁰ d₂₀ 1.5560, ²⁰ n_D 1.4960. ⁴³⁶

BuOP(O)Cl₂. A. ³⁴¹ C (poor). ³⁴¹ Liquid, b₁₇ 90°, b₁₃ 85°, ¹¹ d₄ 1.2711, ²⁵ d₄ 1.2560, ¹¹ n_D 1.4453. ³⁴¹

B. ALKYL DIHALOTHIONOPHOSPHATES. $\text{ROP}(\text{S})\text{X}_2$

EtOP(S)F₂. D. Liquid, b. 78.4°, f.p. –124°, ⁰ d₄ 1.3019. ¹¹⁴

EtOP(S)FCl. D. Liquid, dec. 100°, b₂₀ 26.2°, f.p. –178°, ⁰ d₄ 1.3828. ¹¹⁴

MeOP(S)Cl₂. A. Liquid, b₄₀ 70°, ⁰ d₀ 1.4949. ^{400, 402}

EtOP(S)Cl₂. A. Liquid, b₂₀ 52° ¹¹⁴ (older values, b₂₀ 68°, ⁰ d₀ 1.3966, ^{400, 402} appear to be questionable); f.p. –78.4°, ⁰ d₄ 1.4395. ¹¹⁴

PrOP(S)Cl₂. A. Liquid, b₂₀ 84°, b₂₀ 80°, ⁰ d₀ 1.3344. ^{400, 402}

242 PHOSPHATES, HALOPHOSPHATES, AND THIO ANALOGS

CH₂:CHCH₂OP(S)Cl₂. A.⁴⁰⁶ E.⁴⁰⁵ Liquid, b₂₅ 74°. ^{405, 406}**BuOP(S)Cl₂.** A. Liquid, b₁₀ 81–2°. ³⁵²**iso-BuOP(S)Cl₂.** A. Liquid, b₂₀ 91°, ⁴⁰⁰ b₂₀ 88°, ⁴⁰² d₀⁰ 1.2724. ⁴⁰⁰**iso-AmOP(S)Cl₂.** A. Liquid, b₁₅ 108–9°, d₄⁰ 1.2370, d₄¹⁷ 1.2188. ¹⁸⁵**EtOP(S)Br₂.** A. Liquid, b₂₀ 105°. ⁴⁰²

C. (S)-ALKYL DIHALOTHIOETHIONOPHOSPHATES

EtSP(S)Cl₂. E. Liquid, b₁₀ 92°, d₀⁰ 1.4453. ⁴⁰²D. DIALKYL HALOPHOSPHATES. (RO)₂P(O)X**(MeO)₂P(O)F.** D.³¹⁴**(EtO)₂P(O)F.** A.^{155, 442} D.^{109, 441} F.^{322, 441} Liquid, b. 171°, ¹⁵⁵ b. 168–71°, ⁴⁴² b₄₅ 88–90°, b₂₅ 76–7°, b₂₃ 74–6°, ⁴⁴¹ b₁₈ 70–2°, ^{155, 441} b₁₆ 66–7°, ¹⁰⁹ b₁₂ 63°, ⁴⁴¹ b₁₁ 61–2°. ¹⁰⁹**(FCH₂CH₂O)₂P(O)F.** A. Liquid, b₁₃ 125–7°. ¹⁵⁵**(ClCH₂CH₂O)₂P(O)F.** A. Liquid, b₁₅ 142–4°. ¹⁵⁵**(PrO)₂P(O)F.** A. Liquid, b₂₀ 98–100°. ¹⁵⁵**(iso-PrO)₂P(O)F.** A.¹⁵⁵ D.^{314, 441} F.⁴⁴¹ Liquid, b. 183° (calc.), ⁴⁴¹ b₂₅ 84°, ¹⁵⁵ b₁₇ 74–5°, ⁴⁴¹ b₁₆ 73°, ⁴⁴¹ b₉ 62°, b₅ 46°, ³¹⁴ f.p. –82°. ⁴⁴¹**(C₆H₁₁O)₂P(O)F.** A. Liquid, b_{0.02} 90–6°. ¹⁵⁵**(2-Me·C₆H₁₀O)₂P(O)F.** A. Liquid, b_{0.15} 137°, b_{0.1} 120°. ¹⁵⁵**(EtO)(BuO)P(O)F.** A. Liquid, b₁₈ 83°. ¹⁰⁹**(Et₃PbO)₂P(O)F.** F. Colorless solid, m. about 260° (from EtOAc). ⁴⁴²**(MeO)₂P(O)Cl.** B. Liquid, b_{20–5} 75–80°, b₄ 60°. ³¹⁴**(EtO)₂P(O)Cl.** A.^{388, 432, 438} B.^{41, 345, 438} H.³⁵² Liquid, b₁₈ 93–5°, ³⁴⁵ b₁₀ 93–4°, ⁴³⁸ b₈ 80–2°, ³⁸⁸ b_{2.5} 61–3°. ³⁵²**(EtO)₂P(O)CN.** From isomerization of (EtO)₃P by ICN. (Reaction of KCN with corresponding chlorophosphate is poor.) ⁴⁴² Liquid, b₁₄ 95–7°, b₁₁ 90–1°. ⁴⁴²**(EtO)₂P(O)SCN.** By heating the chlorophosphate with KSCN (besides a by-product, which b₁₃ 112–6°). Liquid, b₁₃ 40°. ⁴⁴² (The reported value appears to be much too low.)**(ClCH₂CH₂O)₂P(O)Cl.** B. Liquid, b₅ 137–9°, d₄²⁰ 1.4623, n_D²⁰ 1.4742. ²⁹²**(iso-PrO)₂P(O)Cl.** B. Liquid, b₁₄ 95–6°, ^{41, 314, 345} b_{0.08} 41°. ³⁴⁵**((ClCH₂)₂CHO)₂P(O)Cl.** B. Liquid, b₂ 182–6°. ¹⁷⁷**(Cl₃C·CHMeO)₂P(O)Cl.** I. Undistillable oil. ²⁶¹**(EtO₂C·CHMeO)₂P(O)Cl.** B. Liquid, b_{0.02} 120°. ¹⁷⁷**(BuO)₂P(O)Cl.** B. C (poor). Liquid, b₁₅ 132–5°, d₄¹⁴ 1.0822, n_D¹⁵ 1.4335. ²⁴¹**(iso-BuO)₂P(O)Cl.** B. Liquid, b_{0.1} 57°. ¹⁷⁷**(iso-AmO)₂P(O)Cl.** B. Liquid, b_{0.02} 74°. ¹⁷⁷**(Et₂CHO)₂P(O)Cl.** B. Liquid, b_{0.1} 73.5°. ¹⁷⁷**(Me₂CH·CH₂·CHMeO)₂P(O)Cl.** B. Liquid, b_{0.01} 72.5–3.5°. ¹⁷⁷**Di-1-(1-chloro-d-galactose-penta-acetate)-chlorophosphate.** I. Solid. ⁴⁹⁶
(n-C₁₆H₃₃O)₂P(O)Cl. A. Crude solid. ⁴⁰⁹**(PhCH₂O)₂P(O)Cl.** B.^{41, 42} J.¹⁸⁷ Undistillable liquid.**(MeO)(ClCH₂CH₂O)P(O)Cl.** B. Liquid, b₈ 88.5°, d₄²⁰ 1.4135, n_D²⁰ 1.4468. ⁴⁹⁶**(EtO)(ClCH₂CH₂O)P(O)Cl.** B. Liquid, b_{4.5} 105–7°, d₄²⁰ 1.3184, n_D²⁰ 1.4426. ⁴⁹⁶E. DIALKYL HALOTHIONOPHOSPHATES. (RO)₂P(S)X**(MeO)₂PSCl.** C. Liquid, b₁₆ 66°, d₄⁰ 1.3414, d₄¹⁷ 1.3217. ¹⁸⁵**(EtO)₂P(S)Cl.** H.³⁶² K.^{110, 216, 225} Liquid, b₂₅ 96–9°, ³⁶² b₁₀ 85°, ¹¹⁰ b₇ 71.5–72°, ²²⁵ b₈ 62°, ¹¹⁰ n_D²⁵ 1.4684. ²²⁵**(BuO)₂P(S)Cl.** H. Liquid, b₂ 95–8°. ³⁶²

F. DI-(S,S)-ALKYL HALODITHIOPHOSPHATES. $(RS)_2P(O)X$ (EtS)₂P(O)F. G. Liquid, b_{15} 104–7°. ¹⁵⁵(EtS)₂P(O)Cl. H. ³⁵² L. ¹⁹⁰ Liquid, b_{22} 145–50°, b_{11} 125°. ¹⁹⁰G. DI-(S,S)-ALKYL HALODITHIOTHIONOPHOSPHATES. $(RS)_2P(S)X$ (EtS)₂P(S)Cl. H. Liquid, b_2 110–3°. ³⁵²

II. COMPOUNDS WITH ESTER BOND TO AN AROMATIC CARBON

A. ARYL DIHALOPHOSPHATES. $ArOP(O)X_2$ PhOP(O)Cl₂. A. ^{265, 287, 421} O. ¹⁵ Also from potassium phenyl sulfate on being heated with phosphorus pentachloride. ⁴⁵⁴ Liquid, b , 241–3°, ^{287, 421} b , 240°, ^{227, 409} b_{21} 130–4°, ²⁸⁷ b_{14} 138–40°, ⁴⁸ b_{11} 121–2°, ^{287, 421} d_4^{20} 1.41214. ^{287, 421}2-Cl-C₆H₄OP(O)Cl₂. M. Yellow oil, b_{12} 135–7°. ²¹4-Cl-C₆H₄OP(O)Cl₂. A. ^{434, 509} J. ³⁰⁰ M. ^{27, 300} Liquid, b , 265°, ²⁷ b_{12} 141°, ²⁷ b_{11} 142°, ⁵⁰⁹ $b_{0.1}$ 95–115°. ⁴³⁴2-MeOC₆H₄OP(O)Cl₂. A. ⁴⁶ O. ¹⁹⁵ Liquid, b_{30} 178–80°. ⁴⁶2-PhOC₆H₄OP(O)Cl₂. A. Liquid, b_{11} 195–8°. ²⁶⁶2-Cl-4-PhO-C₆H₃OP(O)Cl₂. A. Oil, b_{11} 216–9°. ²⁶⁶2-MeC₆H₄OP(O)Cl₂. A. Liquid, b_{19} 135–6°, ¹⁰⁰ b_{15} 127°. ⁹⁷4-MeC₆H₄OP(O)Cl₂. A. Liquid, b , 255°, ⁴²¹ b_{12} 145–50°. ⁴⁸4-Cl-3-MeC₆H₃OP(O)Cl₂. A. Liquid, $b_{0.1}$ 95°. ⁴³⁴2-iso-Pr-5-MeC₆H₃OP(O)Cl₂. A. Liquid, b_{300} 246–9°. ¹⁸⁹2-iso-Pr-6-Cl-5-MeC₆H₂OP(O)Cl₂. A. Liquid, b_{12} 168°. ⁴³⁴4-Bu-2-MeC₆H₃OP(O)Cl₂. A. Liquid, $b_{0.4}$ 128–33°. ⁴³⁴2-Me-6-Pr-CO-C₆H₃OP(O)Cl₂. A. Liquid, $b_{0.2}$ 167°. ⁴³⁴6-Bu-2-iso-Pr-5-MeC₆H₂OP(O)Cl₂. A. Liquid, $b_{0.2}$ 138–41°. ⁴³⁴4-iso-Am-2-MeC₆H₃OP(O)Cl₂. A. Liquid, $b_{0.3}$ 125–33°. ⁴³⁴4-(*n*-C₆H₁₃)-2-MeC₆H₃OP(O)Cl₂. A. Liquid, $b_{0.15}$ 140–5°. ⁴³⁴4-*tert*-Bu-C₆H₄OP(O)Cl₂. A. Liquid, b_{10} 176°, b_6 150–3°, d_4^{20} 1.244. ⁹⁸4-*tert*-Am-C₆H₄OP(O)Cl₂. A. Liquid, b_{10} 174°, d_4^{25} 1.159. ⁹⁸4-*tert*-C₆H₁₇-C₆H₄OP(O)Cl₂. A. Liquid, b_{13} 197–203°, b_{10} 192–5°. ⁹⁸5-Chlorocarvacryl dichlorophosphate. A. Liquid, $b_{0.6}$ 123–5°. ⁴³⁴1-C₁₀H₇OP(O)Cl₂. A. Liquid, b , 325–7°, b_{20} 198–200°. ³²¹2-C₁₀H₇OP(O)Cl₂. A. Crystals, m , 39°, b_{20} 204–5°. ³²¹2-PhC₆H₄OP(O)Cl₂. A. Liquid, b_{47} 228°. ⁹⁷3-PhC₆H₄OP(O)Cl₂. A. Liquid, b_9 218–21°. ¹²⁰4-PhC₆H₄OP(O)Cl₂. A. Crystals, m , 83°, b_{12-3} 211–23°. ¹²¹Cholesteryl dichlorophosphate. H. Crystals, m , 122°. ²¹²6''-(2,2,5',4''-Tetramethyl-3',4',5',6'-tetrahydro-dibenzopyran)-dichlorophosphate. H. Viscous mass, $b_{0.15}$ 170°. ¹⁰⁴Tetrahydrocannabinyl dichlorophosphate. H. Liquid, $b_{0.1}$ 185°. ¹⁰⁴

B. BIS-DIHALOPHOSPHATES

1,3-C₆H₄O₂(POCl₂)₂. A. Liquid, b_{115} 263°, b_{75} 216°, d_4^{15} 1.643. ³¹¹1,4-C₆H₄O₂(POCl₂)₂. A. Crystals, m , 123°, b_{70} 270°. ³¹¹

C. DERIVATIVES OF HYDROXYBENZOIC ACIDS

2-CICOC₆H₄OP(O)Cl₂. M. ^{10, 15, 17, 179} N. ¹⁴ Liquid, b_{11} 168°, d_4^{20} 1.55873.3-CICOC₆H₄OP(O)Cl₂. M. Liquid, b , 315–22°, b_{11} 168–70°, d_4^{20} 1.54844. ¹⁷4-CICOC₆H₄OP(O)Cl₂. M. Liquid, b_{13} 176°, d_4^{20} 1.54219. ¹⁷

244 PHOSPHATES, HALOPHOSPHATES, AND THIO ANALOGS

- 2-ClCO-4-ClC₆H₃OP(O)Cl₂.** M.^{9,13} N.¹³ Liquid, b₁₃ 183–4°.¹³
2-ClCO-6-ClC₆H₃OP(O)Cl₂. N. Liquid, b₁₃ 195–6°.¹³
2-ClCO-4-MeC₆H₃OP(O)Cl₂. M. N. Liquid, b₁₂ 185°.²⁰
2-ClCO-5-MeC₆H₃OP(O)Cl₂. M. N. Liquid, b₁₂ 184.6–5.4°.²⁰
2-ClCO-6-MeC₆H₃OP(O)Cl₂. N. Liquid, b₁₂ 185.6–6.2°.^{11,28}
1-ClCO-C₁₀H₆-(2)-OP(O)Cl₂. M. Needles, m. 38° (from ligroin).⁴¹⁷
3-ClCO-C₁₀H₆-(2)-OP(O)Cl₂. M. Needles, m. 63°.²⁶⁷

D. DERIVATIVES OF HYDROXYBENZOIC ACIDS WHICH MAY BE EITHER Cl₃C-ArOP(O)Cl₂ OR ClCO-ArOPCl₄

- 2-Cl₃CC₆H₄OP(O)Cl₂.** M. Liquid, b₁₁ 178–9°, d₄²⁰ 1.62019.¹⁷
3-Cl₃CC₆H₄OP(O)Cl₂. M. Liquid, b₁₁ 178°.¹⁷
2-Cl₃C-4-ClC₆H₃OP(O)Cl₂. M. Crystals, m. 59–60°, b₁₅ 197°.¹³
2-Cl₃C-4,6-Cl₂C₆H₂OP(O)Cl₂. M. Crystals, m. 102–4° (from Me₂CO).¹⁶
2-Cl₃C-4,6-Br₂C₆H₂OP(O)Cl₂. M. Plates, m. 129–30° (from ligroin).¹⁸
2-Cl₃C-4,6-I₂C₆H₂OP(O)Cl₂. M. Crystals, m. 126° (from ligroin).¹⁹
2-Cl₃C-6-MeC₆H₃OP(O)Cl₂. M. Plates, m. 80°, b₁₃ 199.4–9.8°.²⁰
2-Cl₃C-C₁₀H₆OP(O)Cl₂. M. Prisms, m. 115° (from ligroin).^{493,494}

E. DERIVATIVES OF HYDROXSULFONIC ACIDS

- 2-ClSO₂C₆H₄OP(O)Cl₂.** M. Liquid.²¹
4-ClSO₂C₆H₄OP(O)Cl₂. M. Needles, m. 87–8°, b_{13.5} 203°.¹²
4-ClSO₂-2,6-Br₂C₆H₂OP(O)Cl₂. M. Crystals, m. 76–8°.¹² m. 69–70°.²⁷
2-ClSO₂-6-Br-4-MeC₆H₂OP(O)Cl₂. M. Prisms, m. 147° (from ligroin).⁵¹⁴

F. ARYL DIHALOTHIONOPHOSPHATES. ArOP(S)X₂

- PhOP(S)Cl₂.** A.³⁵⁷ E.^{15,210} K.^{51,53} Liquid, b₂₂ 133°.²¹⁰ b₁₆ 132°.²¹⁰ b₁₅ 133–5°.⁵³ b₁₁ 119–20°.¹⁵ d₄²⁰ 1.40593.²¹⁰
4-ClC₆H₄OP(S)Cl₂. E. Liquid, b₁₁ 143–5°.⁴⁵⁵
2-MeC₆H₄OP(S)Cl₂. E. Liquid, b₁₅ 130–1°.⁴⁵⁵
3-MeC₆H₄OP(S)Cl₂. E. Liquid, b₁₂ 138°.⁴⁵⁵
4-MeC₆H₄OP(S)Cl₂. E.⁴⁵⁵ K.⁵³ Liquid, b₁₂ 138°.⁵³ b₁₁ 135–6°.⁴⁵⁵
PhOP(S)Br₂. E. Liquid, b₁₁ 156–7°.⁴⁵⁵

G. (S)-ARYL DIHALOTHIOHOPHOSPHATES. ArSP(S)X₂

- PhSP(S)Cl₂.** E. Liquid, b₁₆ 168–70°.³⁵⁹

H. DIARYL HALOPHOSPHATES. (ArO)₂P(O)X

- (PhO)₂P(O)F.** G.¹⁵⁵ (An earlier preparation, D,²⁴⁹ is in error.) Liquid, b_{0,07} 106–8°, b_{0,4} 115–8°.¹⁵⁵
(PhO)₂P(O)Cl. A. Liquid, b₂₇₂ 314–6°, b₂₁₆ 275°.⁴²¹ b₂₁ 212–5°.^{305,327,365} b₁₃₋₄ 195°.¹⁵ d₄²⁰ 1.29604.²⁶⁵
1,2-C₆H₄O₂P(O)Cl. C.^{24,311} O.^{22,24} Needles, m. 59–60°.²⁴ m. 58–9°.²² b₅₅ 162°.³¹¹ b₉ 150°.²⁴ b₁₂ 122°(??).²²
(4-ClC₆H₄O₂)P(O)Cl. A.^{375,434,509} J.⁴⁷ Needles, m. 53–4°.³⁷⁵ b₁₅ 225–6°.³⁷⁵ b_{0,1} 164–76°.⁴³⁴
(2,4,6-Cl₃C₆H₃O)₂P(O)Cl. I. Crystals, m. 126–9° (from benzene).²²
(2-MeOC₆H₄O)₂P(O)Cl. A.⁴⁶ O.¹⁹⁵ Liquid, b₁₅ 258°.⁴⁶
(4-Cl-3-MeC₆H₃O)₂P(O)Cl. A. Liquid, b_{0,1} 170°.⁴³⁴
(4-tert-BuC₆H₄O)₂P(O)Cl. A. Crystals, m. 100–1.5°, b₁₀ 190–310° (crude).⁹⁰
(2-iso-Pr-5-MeC₆H₃O)₂P(O)Cl. A. Liquid, b₃₂₀ 330–40°.¹⁸⁹

(2-iso-Pr-5-Me-6-ClC₆H₂O)₂P(O)Cl. A. Liquid, b_{0,2} 185–95°. ⁴³⁴
 (4-Bu-2-MeC₆H₃O)₂P(O)Cl. A. Liquid, b_{0,4} 219–23°. ⁴³⁴
 (4-iso-Am-2-MeC₆H₃O)₂P(O)Cl. A. Liquid, b_{0,2} 215–22°. ⁴³⁴
 (4-n-C₆H₁₃)-2-MeC₆H₃O)₂P(O)Cl. A. Liquid, b_{0,1} 245–52°. ⁴³⁴
 Di-(5-chlorocarvacryl) chlorophosphate. A. Liquid, b_{0,6} 190–2°. ⁴³⁴
 Di-(6-butylthymyl) chlorophosphate. A. Liquid, b_{0,2} 218–30°. ⁴³⁴
 (4-tert-C₈H₁₇-C₆H₄O)₂P(O)Cl. A. Viscous mass, b₁₀₋₃ 203–20°. ⁹⁸

(EtO)(PhO)P(O)Cl. A. Crude, undistillable oil. ³⁶⁸
 (PhO)(2-MeC₆H₄O)P(O)Cl. A. Liquid, b₁₁ 200–12°. ⁹⁷
 (PhO)(4-MeC₆H₄O)P(O)Cl. K. Liquid, b₃₅ 244–8°. ³⁴⁰
 (PhO)(2-C₁₀H₇O)P(O)Cl. A. K. Liquid, b₂₉ 286°. ³⁰⁹
 2,2'-(1,1'-Dinaphthylene) chlorophosphate. A. Crystals. ³⁵⁰

I. DIARYL HALOTHIONOPHOSPHATES. (ArO)₂P(S)X

(PhO)₂P(S)Cl. A. ⁵⁸ E. ^{15, 208, 248, 455} K. ^{51, 53, 375} Needles, m. 68°, ^{208, 455} m. 67°, ⁵³ m. 66–7°, ⁵¹ m. 64°, ²⁴⁸ m. 63–4°, ¹⁵ m. 53°, ³⁷⁵ b₁₁ 194°, ⁵³ b₁ 180–3°. ²⁴⁸
 1,2-C₆H₄O₂P(S)Cl. F. Needles, m. 49–50° (from EtOH), b₁₁ 106°. ²³
 4-Me-1,2-C₆H₃O₂P(S)Cl. E. Liquid, b₁₁ 142–3°. ³⁰
 (2-MeC₆H₄O)₂P(S)Cl. E. Liquid, b₁₁ 212°. ⁴⁵⁵
 (3-MeC₆H₄O)₂P(S)Cl. E. Needles, m. 33–4°, b₁₁ 218°. ¹²⁵
 (4-ClC₆H₄O)₂P(S)Cl. E. Crystals, m. 43–4°, b₁₁ 243–5°. ⁴⁵⁵ An older preparation, K. ⁵¹ is erroneous.
 (4-MeC₆H₄O)₂P(S)Cl. E. ⁴⁵⁵ K. ^{51, 53} Crystals, m. 53°, ^{51, 53} m. 54–5°. ⁴⁵⁵
 (PhO)₂P(S)Br. E. Needles, m. 72.5° (from EtOH), b₁₁ 200°. ⁴⁵⁵

J. DIARYL HALOSELENOPHOSPHATES. (ArO)₂P(Se)X

(PhO)₂P(Se)Cl. E. Needles, m. 59–9.5° (from MeOH), b₁₁ 200°. ⁴⁵⁵
 (4-ClC₆H₄O)₂P(Se)Cl. E. Crystals, m. 59–61° (from ligroin), b₁₁ 245°. ⁴⁵⁵
 (2-MeC₆H₄O)₂P(Se)Cl. E. Crude liquid, b₁₁ 224–7°. ⁴⁵⁵
 (4-MeC₆H₄O)₂P(Se)Cl. E. Needles, m. 48–9°, b₁₁ 235°. ⁴⁵⁵
 (PhO)₂P(Se)Br. E. Crystals, m. 64–5° (from ligroin). ⁴⁵⁵

PHOSPHATES AND THIOPHOSPHATES

I. PRIMARY ESTERS

A. COMPOUNDS WITH THE ESTER LINKAGE ON ALIPHATIC CARBON

1. HYDROCARBON DERIVATIVES AND THEIR HALO DERIVATIVES

MeOPO(OH)₂. I. ^{151, 259, 339} II. ¹⁶¹ III. ⁴⁴⁵ V. ^{72, 73} Disodium salt. ⁷² Barium salts. ^{72, 73, 151, 259} Calcium salts. ⁷² Lead salt. ³⁵⁹
 MeOPSO₂H₂. XVIIA. ²⁰² XVIII. ^{400, 402} Disodium salt (6H₂O), m. 49°. ²⁰²
 EtOPO(OH)₂. I. ^{151, 239, 409, 473} II. ^{161, 165, 322, 335, 395} V. ^{72, 73, 186} IX–XVIIIB. ^{41, 43} XIII. ³⁷⁴
 XIII–XVIIIB. ⁴² XVI. ^{88, 323} Barium salts. ^{88, 145, 395} Calcium salts. ^{72, 407}
 EtOPSO₂H₂. III. ^{163, 172, 402} Barium salt. ^{163, 172} Silver salt. ⁴⁰²
 ClCH₂CH₂OPO(OH)₂. III. ²⁶¹ VI. ^{320, 409} XVI. ³²³ Barium salt. ^{220, 251, 323}
 BrCH₂CH₂OPO(OH)₂. V. ⁵⁰⁸ Barium salt. ⁵⁰⁸
 PrOPO(OH)₂. V. ⁷² XIX. ⁴⁰⁹ Calcium salt. ⁷² Barium salt. ^{152, 409}
 PrOPSO₂H₂. III. ⁴⁰² Sodium salt. ⁴⁰²
 CH₂:CH·CH₂OPO(OH)₂. I. ^{146, 147, 151} V. ^{72, 147, 508} Calcium salt. ⁷² Barium salt. ^{72, 144, 147}
 BrCH₂CH₂CH₂OPO(OH)₂. V. ⁵⁰⁸ Barium salt. ⁵⁰⁸

iso-PrOPO(OH)₂. V.⁷² Calcium salt.⁷² Barium salt.¹⁵²

BuOPO(OH)₂. XIII-XVII B.⁴¹ Barium salt.⁴¹

iso-BuOPO(OH)₂. V.⁷² Calcium salt.⁷² Barium salt.¹⁵²

iso-AmOPO(OH)₂. II. Copper salt.²⁵⁸

iso-AmOPSO₂H₂. III. Sodium salt: barium salt.¹⁶²

n-C₁₆H₃₃OPO(OH)₂. I.¹⁰⁷ II.¹⁶¹ III.^{164, 251, 482} XVI.⁴⁰⁹ Crystals (from EtOH or AcOH), m. 73–6°, ⁴⁸² m. 72°, ^{107, 409} m. 71°. ¹⁶⁴ Barium salt, said to be water-soluble, ⁴⁰⁹ actually is insoluble.^{164, 251} Acid sodium salt, m. 178–9° (from AcOH).⁴⁸² Piperazine salt (4H₂O), m. 229–30°. ⁴⁸² The free acid has tetrameric molecular weight in camphor.⁴⁸²

Hydnocarpyl- and chaulmoogryl phosphates, their dihydro derivatives, and oleyl phosphate are described as waxy solids, which do not have definite melting points. I.¹⁵¹

PhCH₂OPO(OH)₂. V.⁵⁰⁸ XVI.³²³ Barium salt.^{323, 508}

EtHgOPO(OH)₂. By heating the secondary ester with alcoholic phosphoric acid. Crystals, m. 115° (from EtOH).⁷

CH₂(OPO₃H₂)₂. The original preparation has been disclaimed.¹⁷⁶

2. HYDROXY COMPOUNDS AND SIMPLE DERIVATIVES

MeCO·OCH₂OPO(OH)₂. V. Calcium salt.⁴¹⁶

HOCH₂CH₂OPO(OH)₂. II.^{135, 140} V.⁴⁰⁹ XII.⁴² By boiling the 2-chloro analog with lead oxide in water.⁴⁰⁹ Sodium salt, m. 61° (hexahydrate).⁴⁰⁹ Barium salt (monohydrate).^{42, 135, 140} Calcium salt.¹⁴⁰ Silver salt.⁸⁵

MeO·CH₂CH₂OPO(OH)₂. I. Calcium salt. Barium salt.⁵⁵

Me·CHOH·CH₂OPO(OH)₂. XII. Silver salt.⁴²

ClCH₂·CHOH·CH₂OPO(OH)₂. XII.^{74, 76, 507} Barium salt.⁷⁴

ICH₂·CHOH·CH₂OPO(OH)₂. V.^{507, 508} XII.¹⁹⁹ Calcium salt.¹⁹⁹ Barium salt.⁵⁰⁸

HOCH₂·C(NO₂)(CH₂OH)·CH₂OPO(OH)₂. VI.⁵¹⁰ Barium salt.⁵¹⁰

Mannityl phosphate (position unknown). I.⁴⁵⁰ II.¹³⁵

Dulcitol phosphate (position unknown). II. Barium salt.¹⁴¹

Citronellal phosphate. XIIA. Plates, m. 203° (from EtOH).¹⁹¹

4-Hydroxy-tetrahydrofuryl-3-phosphate. II.¹³⁵ Barium salt.

GLYCEROPHOSPHATES

Mixed 1- and 2-glycerophosphates. II.^{5, 139, 414, 500} The free acid cannot be obtained by acidification of metal salts; it can be secured from the lead salt by treatment with hydrogen sulfide.¹³⁹ The usual preparation of technical product: I and II procedures (separate or combined).^{5, 138, 161, 231, 397, 411, 415}

1-Glycerophosphate. Inactive: V.⁸⁰ IV-XVIIA.²⁶⁴ IV-XVII B.¹¹⁹ VII.²²⁰ XII.^{220, 507} XII-XVIIA.⁷⁶ Sodium salt.⁷⁶ Barium salt.^{220, 254, 507} Strychnine and quinine salts:²⁹⁶ used for resolution of the racemate.²⁹⁶

L-1-Glycerophosphate. VII (from acetone derivative). Barium salt.⁶⁰ Silver salt.⁶⁰

D-1-Glycerophosphate. VII (from acetone derivative). Barium salt.⁶¹ Silver salt.⁶¹ Ethyl iodide and silver oxide yield the (P)-diethyl ester of the diethyl ether: liquid, b_{0.22} 104–5°, ¹⁹ n_D 1.4252.⁶¹

Substantially the 1-isomer is obtained by: II.^{70, 71, 260} V.³⁰⁸ XII.⁶⁹ (P)-Radioactive form: VII.¹⁵⁶

MeOCH₂·CH(OMe)·CH₂OPO(OH)₂. By hydrolysis of its diethyl ester (above) with 5% HCl. Barium salt.³⁰⁸

2,3-Distearyl-1-glycerophosphate. I. Crystals, m. 71° (from CS_2).²⁵² Not stable on standing.²⁵²

(2,3)-Palmital-1-glycerophosphate (migration not excluded). VI.¹⁰⁶ Needles (from EtOH).¹⁰⁶ Similar acetal of octadecanal is mentioned but not characterized.¹⁰⁶

2-Glycerophosphate. Distinguished from the 1-isomer by the formation of poorly soluble salt with barium nitrate.^{296, 298} IV-XVIIA.¹¹⁹ XVIIA.⁴⁶⁷ II.⁷⁷ II (from glycerol-1,2-dichlorohydrin), followed by hydrolysis with calcium hydroxide.⁴⁶⁷ By hydrolysis of di-2-(1,3-dichloro)propyl phosphate.³⁰⁸ Barium salt.^{119, 298-6, 298, 467} Calcium salt.⁴⁶⁷ Free acid: sirup.^{230, 392}

$(\text{PhOCH}_2)_2\text{CHOPO}(\text{OH})_2$. VI. Crystals, m. $137-7.5^{\circ}$ (from EtOAc-ligroin).

Sodium salt $(10\text{H}_2\text{O})$, m. 54° .¹¹⁵

$(2\text{-MeC}_6\text{H}_4\text{OCH}_2)_2\text{CHOPO}(\text{OH})_2$. VI. Crystals. Sodium salt.¹¹⁵

$(4\text{-MeC}_6\text{H}_4\text{OCH}_2)_2\text{CHOPO}(\text{OH})_2$. VI. Crystals.¹¹⁵

$(n\text{-C}_9\text{H}_{19}\text{CO}\cdot\text{OCH}_2)(\text{HOCH}_2)\text{CHOPO}(\text{OH})_2$. From the parent ester and acyl chloride in pyridine suspension. Sodium salt. Acid barium salt, m. $261-3^{\circ}$.³⁹

$(n\text{-C}_{11}\text{H}_{23}\text{CO}\cdot\text{OCH}_2)(\text{HOCH}_2)\text{CHOPO}(\text{OH})_2$. Prepared as above. Sodium salt. Acid barium salt, m. $245-55^{\circ}$.³⁹

$(\text{PhCO}\cdot\text{OCH}_2)(\text{HOCH}_2)\text{CHOPO}(\text{OH})_2$. VII-XVIIIB (from 1-benzoyl-3-trityl-glycerol). Potassium salt.⁶⁹

$(n\text{-C}_{13}\text{H}_{27}\text{CO}\cdot\text{OCH}_2)_2\text{CHOPO}(\text{OH})_2$. VII.²⁷⁴ Acid quinoline salt, m. $96.6-7.5^{\circ}$ (from EtOAc).²⁷⁴

$(n\text{-C}_{15}\text{H}_{31}\text{CO}\cdot\text{OCH}_2)_2\text{CHOPO}(\text{OH})_2$. From the parent ester and the acyl chloride in pyridine. Silver salt.²⁹³

1,3-Dichaulmoogryl-2-glycerophosphate. VI. Lead salt, m. 175° . Choline salt, m. $160-5^{\circ}$. Sodium salt, m. $149-50^{\circ}$.⁴⁷⁹

$\text{HOCH}_2\text{CH}(\text{OPO}_3\text{H}_2)\text{CHOPO}(\text{OH})_2(?)$. II.⁷⁰

$\text{HOCH}(\text{CH}_2\text{OPO}_3\text{H}_2)_2(?)$. XII-II.⁷⁶ Sodium salt.⁷⁶

3. COMPOUNDS WITH CARBONYL GROUPS (ACTUAL OR POTENTIAL)

$\text{OHC}\cdot\text{CH}_2\text{OPO}(\text{OH})_2$. By oxidation of 1-glycerophosphate with iodate. Barium salt.^{226, 227}

Glyceraldehyde phosphate. Either 3- or 2-phosphate: VII (from glyceraldehyde diethyl acetal). Calcium salt.^{93, 221}

3-Glyceraldehyde phosphate. VII-XVIIIB (from the glycerol dibenzyl ether).²²²

IV-XVIIA-B (from glyceraldehyde dimer; the intermediate octaphenyl ester, m. $110-1^{\circ}$,⁶³ m. $108-9^{\circ}$.⁶²).^{64, 223} Calcium salt.⁶⁴

$\text{HOCH}_2\cdot\text{CO}\cdot\text{CH}_2\text{OPO}(\text{OH})_2$. XVI.³²⁴ By oxidation of 1-glycerophosphate with bromine water.²⁵⁰ Barium salt.²⁵⁰

$\text{OC}\cdot(\text{CH}_2\text{OPO}_3\text{H}_2)_2(?)$. XVI. Barium salt.³²⁴

DERIVATIVES OF MONOSACCHARIDES

Glucose phosphate. Uncertain orientation: VI. III.^{8, 392} Lead salt, m. 187° .⁸

D-Glucopyranose-1-phosphate. Alpha form (Cori ester). V (using trisilver phosphate).^{178, 495} Potassium salt. Brucine salt, m. $173-8^{\circ}$. Beta form. V (using silver dibenzyl phosphate) followed by XVIIA.⁴⁹⁵ The dibenzyl ester of the acetate, m. $78-9^{\circ}$. Brucine salt decahydrate, m. $160-5^{\circ}$; anhydrous, m. $162-6^{\circ}$.

L-Glucopyranose-1-phosphate. Alpha form. V (using trisilver phosphate).⁴¹³ Potassium salt. Barium salt.⁴¹³

248 PHOSPHATES, HALOPHOSPHATES, AND THIO ANALOGS

Glucufuranose-3-phosphate. VII-XVIIA.³⁹⁸ Barium salt. The 1,2-acetone derivative and the diacetone derivative isolated as barium salts.³⁹⁸

Glucose-4-phosphate. VII (from 1,2,3,6-tetra-acetylglucose). Barium salt. Brucine salt.⁴²⁵

Glucose-6-phosphate. IV-XVIIIB (from 1,2,3,4-tetra-acetyl glucose; deacetylation performed with potassium methoxide),²²⁴ (from 1,2-acetone-glucose, using dibenzyl chlorophosphate).⁴¹ Tetra-acetate, m. 128° (diphenyl ester, m. 68°).²²⁴ VII (from acetone-glucose).³²⁸ Potassium salt.²²⁴ Barium salt.^{41, 398}

Methyl glucoside: alpha form. VI.^{219, 398} Barium salt.^{219, 398}

Fructose phosphate. Uncertain orientation. XVI.³²⁴ Barium salt. Phenylazone, m. 158°. Has reducing properties.³²⁴

1(?) -Fructose phosphate. IV-XVIIIB (from 2,3,4,5-diacetone-fructose).¹¹⁹ The diphenyl ester of the intermediate, m. 52.5°. Barium salt.¹¹⁹

3(?) -Fructose phosphate. IV-XVIIIB (from 1,2,4,5-diacetone-fructose).¹¹⁹ The diphenyl ester of the intermediate, m. 71-2°, on removal of the acetone residue with 70% acetic acid yields the diphenyl ester of presumably 1,2-acetone derivative, m. 136°. The product has strong reducing properties.¹¹⁹

6-Fructose phosphate. By hydrolysis of the 1,6-diphosphate with dilute acid.³⁷⁸ Barium salt.³⁷⁸

Galactose phosphate. Uncertain structure. III.³⁸¹ Calcium salt.

D-Galactose-1-phosphate. Beta form. V (from bromotetra-acetate; acetate groups removed with sodium ethoxide).⁴²⁷ Barium salt.^{315, 427}

Xylose phosphate.

Xylose-1-phosphate. V (from bromotriacetate).³⁵³ Barium salt. Potassium salt. Periodate oxidation indicates structure of D-xylopyranose-1-phosphate.³⁵³

Xylose-5-phosphate. VII.³²⁹ Barium salt.³²⁹

Arabinose-5-phosphate. VII.³²⁷ Barium salt. Brucine salt.³²⁷

Maltose-1-phosphate. V, followed by XVIIA.³⁵³ Barium salt. The periodate oxidation indicates the structure of glucopyranosido-4-glucopyranose-1-phosphate. Does not decompose Fehling solution.³⁵³

4. COMPOUNDS WITH CARBOXYL GROUPS

HO₂C·CH₂OPO(OH)₂. By oxidation of the aldehyde derivative by hypiodite.²²⁶

Isolated either as a poorly soluble barium salt (4H₂O) or quinine salt, m. 148-9°. ²²⁸

The compound is more stable to hydrolysis than the aldehyde analog.²²⁸

HO₂C·C(CH₂Ph)₂OPO(OH)₂. XX-III. Prisms, dec. 160° (from water).⁴⁵³

HO₂C·CHMe·OPO(OH)₂. Levo isomer. II.¹⁶¹ VI.⁴⁷⁸ Barium salt (2H₂O; from dil. EtOH).⁴⁷⁸ [α]_D²⁵ -13.6°. ⁴⁸⁰ Sodium salt (from dil. EtOH), [α]_D -9.74°. ⁴⁷⁸

Neutral brucine salt, m. 153-4°; acid brucine salt (4H₂O), m. 166°. ⁴⁸⁰

HO₂C·C(OPO₃H₂):CH₂. VI (from pyruvic acid).³⁰⁶ II.¹⁶¹ Barium salt (from dil. EtOH).³⁰⁶

Phosphoglyceric acid. (1- or 2-phosphate). XVI-XVIIA.^{385, 477} *dl*-Form. Barium salt (from water).³⁸⁶ Partially resolved by means of the brucine salt, with the dextro form having [α]_D 2.4° (in water).⁴⁷⁷

1-phosphate (?). By oxidation of the glycerophosphate with bromine water. Barium and silver salts (from water).³⁰⁶

2-phosphate (?). By oxidation of the glycerophosphate with bromine water. Barium salt.³⁰⁶ The naturally occurring product is a mixture of 1- and 2-phosphates.

D-(−)-1-phosphate. XVI. Some dextro isomer also forms. The levo isomer has $[\alpha]_D^{25} -13.27^\circ$.³⁷⁹

Me·C(OPO₃H₂):CH·CO(OEt). X (from ethyl sodioacetoacetate), followed by de-ethylation by NaOH.²⁹⁴ Sodium salt.²⁹⁴

HO₂C·CH₂CH(OPO₃H₂)·CO₂H. Dextro and levo isomers prepared by IV–XVIIB from corresponding isomers of diethyl malate.²³⁸ Levo isomer: barium salt, $[\alpha]_D^{22} -4.03^\circ$ (in 2 N HCl). Dextro isomer: barium salt, $[\alpha]_D^{23} 4.08^\circ$ (in 2 N HCl).²³⁸ The intermediate (C)-diethyl ester is an oil.²³⁸

HO₂C·CHOH·CH(OPO₃H₂)·CO₂H. Dextro isomer: VI. Barium salt (from dil. EtOH). Benzidine salt.³⁸³

5. DERIVATIVE OF NITROGEN BASES

H₂NCH₂CH₂OPO(OH)₂. II.^{161, 410} III.⁴¹⁰ XII.¹⁶⁴ Crystals, m. 238° (from dil. MeOH).³⁹⁰ m. 233–5°.¹⁶¹ dec. 240°.¹⁶⁴ Barium salt (from dil. EtOH).^{164, 390}

Me₃N(OH)CH₂CH₂OPO(OH)₂. II.^{161, 286, 410} III.⁴¹⁰ IV (from choline chloride), via the diphenyl ester, m. 133–4°.⁶⁶ Barium salt (from dil. EtOH).⁶⁸ Diphenyl ester forms the reineckate, m. 162–4°.⁶⁸ and chloraurate, m. 122°.⁶⁶ The phosphate forms a chloroplatinate, dec. 207–8° (from alc. KCl),²⁸⁶ an adduct with mercuric chloride, m. 180–4° (from 80% EtOH),⁴³¹ and a reineckate,⁴³¹ as well as a calcium salt (from dil. EtOH).^{286, 410, 431}

2-(4-Methyl-5-thiazolyl)ethyl phosphate. II (using pyrophosphoric acid).⁴³³ Crystals, m. 162° (from EtOH–Et₂O). Silver salt.⁴³³

Thiamine phosphate. II (using pyrophosphoric acid and sodium pyrophosphate).⁴³³ Crystals, m. 200–2° (from dil. EtOH–Me₂CO). Silver salt.⁴³³

Threonine phosphate. II. Plates, dec. 169° (from dil. EtOH). Lead salt.⁴⁰⁸

Serine-3-phosphate. II.^{331, 332, 408} In poor yield by VII,³³¹ from benzylidene-serine. The *dl*-compound resolved by brucine salt (dec. 130°).³³² and the dextro isomer yield a barium salt identical with that of natural product, $[\alpha]_D^{25} 9.4^\circ$. Free acid: plates, dec. 165–6° (from dil. EtOH).⁴⁰⁸ Lead salt.⁴⁰⁸

Lactoflavine-5'-phosphate. VI (from triacetylactoflavine). Sodium salt (from water).³¹⁹

Guanosine-5'-phosphate. VI. VII. Yields are poor when pyridine is used with (PhO)₂POCl. Use of barium hydroxide yields the 3'-isomer.²⁵⁴

Cytidine-2'-phosphate. IV could not be used, as diphenyl chlorophosphate also reacts with the amino group and the nitrogen to phosphorus link could not be cleaved satisfactorily. VII (using an excess of POCl₃ with benzylidene-cytidine; the nitrogen to phosphorus by-product is hydrolyzed by hot 0.25 N HCl).²⁵⁶ Prisms, dec. 240–2° (from dil. EtOH). Lead and barium salts.²⁵⁶

Uridine-2'-phosphate. IV–XVIIB.²⁵⁵ Barium salt. Dibrucine salt (4H₂O), m. 180°.²⁵⁵

Uridine-3'-phosphate. IV–XVIIA (from trityluridine).¹¹⁶ Lead salt. Brucine salt, m. 195°.¹¹⁶

Uridine-5'-phosphate. VI (from uridine),²⁵⁴ (from acetone-uridine derivative).^{254, 333} 'III yields this isomer as well as some 3'-phosphate.²⁵⁴ Barium salt.²⁵⁴ Brucine salt.³³³ Hydrolysis rate is identical with that of the natural product.²⁵⁴

Adenosine-5'-phosphate. IV (from 2,3-diacetyl-adenosine)¹¹⁷ or (from 2,3-acetone-adenosine).⁵⁷ VI (from adenosine).^{254, 265} VII (from acetone-adenosine).³³⁴ If IV is used, XVIIB yields either the free acid or the monobenzyl ester (m. 234°),⁵⁷ when dibenzylchlorophosphate is used; the dibenzyl ester, m. 97–8°.⁵⁷ Free acid: needles, m. 190° (from water), $[\alpha]_D^{20} -45.5^\circ$ (in water).⁵⁷ Acridine salt, m. 208°.⁵⁷

250 PHOSPHATES, HALOPHOSPHATES, AND THIO ANALOGS

B. COMPOUNDS WITH THE ESTER LINKAGE TO A CYCLIC NUCLEUS

1. HYDROCARBON DERIVATIVES

- PhOPO(OH)₂**. I.^{102, 428} III.^{285, 284, 287, 409} XVI.⁴⁰⁹ Scales, m. 99.5°; ²⁸⁵ (from CHCl₃) ²⁶⁵ or needles, m. 97–8° (from water).⁴²¹ Ammonium salt, dec. 140–5° (from water). Calcium, barium, and copper salts are poorly soluble in water.⁴⁰⁹ Potassium salt, plates (from dil. EtOH).⁴⁰⁹ Sodium salt, crystals (from dil. EtOH-Et₂O).²³⁷
- PhOPSO₂H₂**. III.⁵¹ Sirup.⁵¹
- 4-MeC₆H₄OPO(OH)₂**. III. Plates, m. 116° (from CHCl₃).⁴²¹
- 2-Me-5-iso-PrC₆H₃OPO(OH)₂**. III. Potassium salt, plates (from EtOH).²⁶³
- 2-iso-Pr-5-MeC₆H₃OPO(OH)₂**. III. Liquid. Barium salt, plates (from dil. EtOH).¹⁸⁹
- 2-Me-4-BuC₆H₃OPO(OH)₂**. III. Crystals, m. 83°.⁴³⁴
- 1-C₁₀H₇OPO(OH)₂**. III. Crystals, m. 142°. Diphenylhydrazine salt, m. 147–8°. Monophenylhydrazine salt, m. 188°.³²¹
- 2-C₁₀H₇OPO(OH)₂**. III. Crystals, m. 167°. Diphenylhydrazine salt, m. 168°. Monophenylhydrazine salt, m. 180°.³²¹ A more satisfactory preparation is X (using (PhO)₂POCl), followed by XVIIB; the product, m. 172–3° (from EtOH-CHCl₃).⁴²
- Menthyl phosphate**. Levo derivative. III. Crystals (monohydrate), m. 82.5°. Lead, silver, calcium, and barium salts are insoluble.³⁶²
- Bornyl phosphate**. Racemic form: VI.^{288, 384} (Some secondary ester, m. 221°, is formed).²⁸⁸ Needles, m. 155–6° (from benzene-petroleum ether).³⁸⁴ *l*-Form: VI. Crystals, m. 156°, [α]_D –22.6° (in EtOH). *d*-Form: VI. Crystals, m. 154–6°, [α]_D 23.3° (in EtOH).³⁸⁴

1A. STEROL DERIVATIVES

- Cholesteryl phosphate**. III.⁴⁰⁹ VI.^{211, 212, 409, 481} Crystals, m. 175°,⁴⁸¹ m. 193° (from MeOH).^{212, 481} m. 195–6°.²¹¹ Associated in solution in hydrocarbon solvents and assigned a pyrophosphate type formulation;⁴⁸¹ this may be seriously questioned. Sodium salt, m. 265–70°, forms on heating with EtONa.⁴⁸¹ Barium salt (4H₂O), plates (from dil. EtOH).⁴⁰⁹
- Tocopheryl phosphate**. Racemic form. VI. Sodium salt, crystals.²⁹⁷ Free acid is sirupy and partly crystalline.²⁹⁷
- Estradiol-3-phosphate-17-propionate**. VII. Crystals, m. 185–7°.⁴⁶²
- Androsterone-3,17-diol-17-phosphate**. VII (from the 3-acetate). Crystals, m. 218.5° (from dil. EtOH), [α]_D²⁰ –42.9° (in EtOH). Sodium salt, crystals.²⁷⁶
- 17-Testosterone phosphate**. VII (from the enol methyl ether, followed by treatment with warm 2 N HCl). Crystals, m. 155–6° (from dil. MeOH), [α]_D²⁰ 71.9° (in MeOH).²⁷⁶
- Estradiol-17-phosphate**. VII. Crystals, m. 216–7° (from EtOH).⁴⁶²
- Tetrahydrocannabinyl phosphate**. VI. Oil.¹⁰⁴

2. SUBSTITUTED DERIVATIVES (EXCEPT CARBOXY)

- 4-ClC₆H₄OPO(OH)₂**. III.^{300, 484, 509} Crystals, m. 80–1° (from EtOH),³⁰⁰ m. 93°.⁴³⁴ Barium salt.³⁰⁰
- 4-BrC₆H₄OPO(OH)₂**. By bromination of the phenyl compound in CHCl₃. Plates, m. 161° (from CHCl₃).⁵⁰⁹
- Pentachlorophenyl phosphate**. By warming PCl₅ with tetrachloro-*p*-benzoquinone ^{92, 513} or hexachloro-1,4-cyclohexadien-3-one with treatment of the product by water.⁹² By heating PCl₅ to 200–10° with tetrachloro-*o*-benzoquinone ⁵¹⁵

or hexachloro-1-cyclohexenedione^{513, 515} followed by water treatment. Plates, m. 203° (anhydrous, from Et₂O-ligroin), m. 224° (monohydrate).^{513, 515}

3-Me-4-ClC₆H₃OPO(OH)₂. III. Crystals, m. 131°. ⁴³⁴

2-Me-3-Cl-5-iso-PrC₆H₂OPO(OH)₂. III. Crystals, m. 148°. ⁴³⁴

3-Me-6-iso-Pr-2-ClC₆H₃OPO(OH)₂. III. Crystals, m. 142°. ⁴³⁴

2-HOC₆H₄OPO(OH)₂. I (from catechol). Needles, m. 139°. ²³⁹

2-MeOC₆H₄OPO(OH)₂. III. XVIIA. ⁴⁶ Needles, m. 94°. Sodium salt, crystals (from 90% MeOH). Acid calcium salt, needles (from water); neutral salt in insoluble. ⁴⁶

2-PhOC₆H₄OPO(OH)₂. III. Crystals, m. 121–3°. ²⁶⁶

2-MeO-4-CH₂:CHCH₂·C₆H₃OPO(OH)₂. III. Prisms, m. 105° (from dry benzene), m. 46–50° (monohydrate; from Et₂O). ¹¹³ On warming with dil. KOH the product isomerizes into propenyl derivative, which forms needles, m. 105–6° (1.5H₂O). ¹¹³

4-HO-2-ClC₆H₃OPO(OH)₂. III. Crystals, m. 98–100°. ²⁶⁵

4-iso-AmOC₆H₄OPO(OH)₂. III. Crystals, m. 55–8°. ²⁶⁵

4-PhCH₂OC₆H₄OPO(OH)₂. III. Crystals, m. 122°. ²⁶⁶

4-PhOC₆H₄OPO(OH)₂. III. Crystals, m. 127–9°. ²⁶⁶

4-O₂NC₆H₄OPO(OH)₂. By nitration of phenyl phosphate with HNO₃ (d. 1.5) in the cold, ⁴²¹ best followed by freezing out the product in CO₂-alcohol bath, followed by extraction with ether and evaporation. ²⁶⁵ Plates, m. 153° (from Et₂O). ²⁶⁵ Less pure product, m. 112° (from water), ⁴²¹ obtained by evaporation of the nitration mixture, after dilution with alcohol, is probably largely the diethyl ester of the above. ²⁶⁵

2,2,5',4''-Tetramethyl-3',4',5',6'-tetrahydro-dibenzopyran-6''-phosphate. III. Solid. Sodium salt. ¹⁰⁴

2-Me-4-PrCO·C₆H₃OPO(OH)₂. III. Crystals, m. 139°. ⁴³⁴

3. DERIVATIVES OF ACIDS

2-HO₂CC₆H₄OPO(OH)₂. III (from the 2-chloroformyl derivative).^{14, 157, 179} XIX (from the 2-chloroformyl derivative).¹⁷⁹ Crystals, m. 140–2°. ^{14, 179}

3-HO₂CC₆H₄OPO(OH)₂. III (from the 3-chloroformyl derivative).¹⁷ Crystals, m. 200–1°. ¹⁷

4-HO₂CC₆H₄OPO(OH)₂. III (from the 4-chloroformyl derivative).¹⁷ Plates, m. 200°. ¹⁷

2-HO₂C-4-ClC₆H₃OPO(OH)₂. III (from the 2-chloroformyl derivative).¹⁸ Powder, m. 161–2°. ¹³

2-HO₂C-4-MeC₆H₃OPO(OH)₂. III (from the 2-chloroformyl derivative).²⁰ Crystals, m. 139.5–40.4°. ²⁰

2-(PhNHCO)-4-MeC₆H₃OPO(OH)₂. XX (from 6-hydroxy-3-methylbenzophenone oxime).⁶⁶ Crystals, m. 187–9° (from dil. EtOH). ⁶⁶

2-HO₂C-5-MeC₆H₃OPO(OH)₂. III (from the 2-chloroformyl derivative).²⁰ Crystals, m. 150°. ²⁰

2-HO₂C-6-Me-C₆H₃OPO(OH)₂. III (from the 2-chloroformyl derivative).²⁸ Crystals, m. 148–9°. ²⁸

2-HO₂CC₁₀H₆-1-OPO(OH)₂. III (from the 2-chloroformyl derivative).⁴⁰⁴ Needles, unstable in aqueous solution. ⁴⁰⁴

1-HO₂CC₁₀H₆-2-OPO(OH)₂. III (from the 1-chloroformyl derivative).⁴¹⁷ Needles, m. 156° (from benzene-Me₂CO). ⁴¹⁷

6-H₃SC₁₀H₆-2-OPO(OH)₂. X. Barium salt, powder. ¹⁴⁷

Phenolphthalein phosphate. VI. Calcium, barium, and lead salts. ²⁰⁷

DERIVATIVES OF HYDROXY AMINO ACIDS

- Hydroxyproline phosphate.** II (from levo isomer).^{332, 408} Needles, m. 130–1° (anhydrous), m. 115° (from dil. EtOH; hydrate).⁴⁰⁸ Lead salt, insoluble powder.⁴⁰⁸ Barium salt, crystals (from dil. EtOH; monohydrate),^{332, 408} $[\alpha]_D^{25} -13.3^\circ$ (in 10% HCl).³³² Brucine salt, m. 180–3°.³³²
- (O)-Phospho-*l*-tyrosine.** II.⁴⁰⁸ III (from formyl-tyrosine).²⁵⁴ VII (from tyrosine ethyl ester or its N-carbobenzoxy derivative).⁴¹² Crystals, m. 225°.⁴⁰⁸ m. 227°.⁴¹² m. 253° (from dil. EtOH);³³⁰ $[\alpha]_D^{20} -8.8^\circ$ (in 2 N HCl),⁴¹² $[\alpha]_D -9.19^\circ$ (in 2 N HCl).⁴⁰⁸ Lead salt.⁴⁰⁸
- (O)-Phospho-serine.** II. Crystals, m. 165–6°. Lead salt.⁴⁰⁸
- (O)-Phospho-threonine.** II. Crystals, m. 169°.⁴⁰⁸
- (O)-Phospho-isoserine.** II. Barium salt.⁴⁰⁸
- Glycyl-(O)-phosphotyrosine.** VII (from the carbobenzoxy derivative).⁴¹² Crystals, m. 224–5° (from dil. EtOH), $[\alpha]_D^{20} 27.9^\circ$ (in N H₂SO₄). Sodium salt.⁴¹²
- (O)-Phospho-tyrosyl-glycine.** VII (from methyl ester of (N-carbobenzoxy-O-acetyl)-tyrosyl-glycine). Crystals, m. 178°, $[\alpha]_D^{23} 20.0^\circ$ (in N H₂SO₄). Barium and lead salts.⁴¹²
- (O)-Phospho-tyrosyl-glycyl-glycine.** VII (from carbobenzoxy-O-acetyl-tyrosyl-glycyl-glycine methyl ester). Crystals, m. 182°, $[\alpha]_D^{23} 5.7^\circ$ (in N H₂SO₄).⁴¹²
- Glycyl-(O)-phospho-tyrosyl-glycine.** VII (from carbobenzoxyglycyltyrosyl-glycine methyl ester). Crystals, m. 198°, $[\alpha]_D^{23} 8.0^\circ$ (in N H₂SO₄). Sodium salt.⁴¹²

4. DIPHOSPHATES

- p*-C₆H₄(OPO₃H₂)₂.** I. Hygroscopic solid, m. 168–9°.²³⁹
- p*-(H₂O₃POC₆H₄CH₂Et)₂.** VI. Colorless solid. Sodium salt.³⁶¹
- m*-Me₂C(OC₆H₄OPO₃H₂)₂.** III. Crystalline powder.¹⁴⁴
- 2-Methyl-1,4-naphthohydroquinone-diphosphate.** III.²¹⁸ VI.²¹⁷ Sodium salt (dihydrate; from aq. pyridine).^{217–8, 235}
- 2-Phetyl-1,4-naphthohydroquinone-diphosphate.** III. Waxy solid.²¹⁸
- 2-Methyl-3-phytyl-1,4-naphthohydroquinone-diphosphate.** VI. A brown solid.²¹⁷
- 2,6-(Diphenylenedioxide)-diphosphate.** VI. Crystals, m. 236°.⁴⁶⁴
- 1,5-(3,7-dimethyl-diphenylenedioxide)-diphosphate.** VI. Crystals, m. 198°.⁴⁶⁴

II. SECONDARY ESTERS

A. COMPOUNDS WITH THE ESTER LINKAGE TO AN ALIPHATIC CARBON

1. HYDROCARBON DERIVATIVES

- (MeO)₂PO(OH).** I.^{140, 151, 259, 339} III.⁴⁴⁵ V.^{72, 73} XVIIA.^{193, 418} Sirup.¹⁵¹ Silver salt.³³⁹ Calcium salt.⁴⁴⁵ Barium salt, soluble in water.^{151, 269} Lead salt, needles, m. 155°.¹⁸¹
- (MeO)₂POSH.** Sodium salt: XXI. Needles (from MeOAc).²³³ Potassium salt: XXI. Needles (from pyridine-Et₂O).²³³ The foregoing are the best methods of synthesis. Less effective preparations: Sodium salt—XVIIA.^{400, 402} Prisms, m. 140° (with decomposition; from EtOH).⁴⁰⁸ Silver salt—XVIII. Needles, dec. 144°.³⁰² dec. 132°.⁴⁰² The free acid is a by-product in the reaction of methanol with P₂S₅; isolated as the lead salt, prisms, m. 100°.³¹⁶ The sodium salt reacts with bromine and yields the corresponding phosphatogen: (MeO)₂PO·S·S·PO(OMe)₂, crystals, m. 30.5–1° (from Et₂O); the corresponding higher phosphatogens are oils.²³³

- (MeO)₂POSeH.** Sodium salt: XXI. Needles (from MeOAc).²²² Potassium salt: XXI. Similar to the above.²²²
- (MeO)₂PS(SH).** XXII. Nickel salt, m. 113°.²²²
- (MeO)(EtO)PO(OH).** XVI. Barium salt.⁸⁸
- (EtO)₂PO(OH).** I.^{149, 151, 269, 474} II.³²³ V.^{72, 78} XVI.^{293, 409} XVIIA.^{198, 339} XIX.⁴⁶⁶ Sirup, b_{0.01} 116–8° (only in pure state), n_D^{25} 1.4146–1.4152.⁴⁶⁶ Sodium salt (trihydrate).^{72–3, 393} Calcium salt (dihydrate).⁷² Barium salt (hexahydrate), crystals (from 80% EtOH).^{72, 151} Lead salt: needles, m. 180°, soluble in water. The barium salt is usually used in fractional crystallization of the mixed mono- and diethyl esters obtained by I.
- (EtO)₂POSH.** III.³⁵² X.⁴⁰² XVIIA.^{352, 400, 402} XVIII.^{400, 402} XXI.²³² XXII,¹³⁸ identity questionable. Potassium salt, m. 197° (from EtOH).³⁵² Ammonium salt, needles (from MeOH).⁴⁰² Sodium salt, crystals, m. 181°.⁴⁰² Silver salt, prisms, m. 82° (from Et₂O or EtOH).^{400, 402} Double salt with mercuric chloride, m. 66°.⁴⁰²
- (EtO)₂POSeH.** XVIIA.⁴⁰² XXI.²³² Sodium salt, needles, m. 146°.⁴⁰² (from CHCl₃-Et₂O).²³² Potassium salt, needles (from EtOAc).²³² Lead salt, oil.⁴⁰²
- (EtO)₂PS(SH).** III.³⁵² XXII.^{349, 402} Oil. Lead salt, needles, m. 74° (from Et₂O).^{352, 402} forms an adduct with ethyl iodide, m. 73°.⁴⁰² Potassium salt, m. 152–3° (from EtOH-Et₂O).³⁵² Nickel salt, m. 105°.³⁴⁹ Cobalt salt, m. 140°.³⁴⁹ Ferric salt, m. 129°.³⁴⁹
- (EtO)(EtS)POSH.** XVIIA (from (EtO)₂(EtS)PS and NaSEt).⁴⁰² Sodium salt.⁴⁰² Lead salt, oil.⁴⁰² Silver salt, infusible solid.⁴⁰²
- (EtS)₂POSH.** XVIIA (from (EtS)₃PS and EtONa, or (EtS)₂(EtO)PS and alcoholic NaSEt).⁴⁰² Lead salt, glass, soluble in organic solvents.⁴⁰²
- (PrO)₂PO(OH).** V.⁷² XVI.⁴⁰⁹ XVIIA.¹⁹³ Barium salt, needles (from EtOH).⁴⁰⁹ Lead salt, needles, m. 145–7°.¹⁵²
- (PrO)₂POSH.** III.⁴⁰² XVIII.⁴⁰² XXI.²³² Silver salt, needles, m. 124°.⁴⁰² Sodium salt, crystals.⁴⁰² (from ligroin).²³² Potassium salt, needles (from PrOH-Et₂O).²³²
- (PrO)₂POSeH.** XXI. Sodium salt, needles (from ligroin). Potassium salt, needles (from CHCl₃-Et₂O).²³²
- (CH₂:CH·CH₂O)₂PO(OH).** I.^{76, 151} XVIIA.¹⁴⁸ Barium salt, crystals, fairly soluble in water.¹⁴⁸ Lead salt, crystals, m. 151°.¹⁴⁸ Free acid is a sirup.¹⁵¹ Potassium salt, crystals.⁷⁶
- (iso-PrO)₂POSH.** Sodium salt: XXI. Needles (from ligroin).²³² Potassium salt: XXI. Needles (from CHCl₃-Et₂O).²³²
- (iso-PrO)₂POSeH.** Sodium salt: XXI. Needles (from ligroin).²³² Potassium salt: XXI. Needles (from CHCl₃-Et₂O).²³²
- (BuO)₂POSH.** Potassium salt: XXI. Needles (from CHCl₃-Et₂O).²³²
- (BuO)₂POSeH.** Potassium salt: XXI. Needles (from benzene-ligroin).²³²
- (BuO)₂PS(SH).** Potassium salt: III.³⁵² Mercury salt: XXII or from the potassium salt. Needles, m. 61–2° (from MeOH).³⁵²
- (EtO)(iso-BuO)POSH.** III. Isolated as the silver salt, m. 149°.⁴⁰²
- (iso-BuO)₂POSH.** X (by-product).⁴⁰² XVIIA.⁴⁰² XVIII.⁴⁰² XXI.²³² Silver salt, needles, m. 160° (from MeOH-Et₂O).⁴⁰² Potassium salt, needles (from CHCl₃-Et₂O).²³²
- (iso-BuO)₂POSeH.** Potassium salt: XXI. Needles (from benzene-ligroin).²³²
- (iso-BuO)₂PS(SH).** XXII. Nickel salt, m. 63°.³⁴⁹
- (iso-AmO)₂PO(OH).** III. Silver salt. Calcium salt.³¹⁷
- (iso-AmO)₂POSH.** Potassium salt: XXI. Needles (from CHCl₃-Et₂O).²³²
- (iso-AmO)₂POSeH.** Potassium salt: XXI. Needles (from CHCl₃-Et₂O).²³²
- (iso-AmO)₂PS(SH).** XXII. Sirup. Lead salt, prisms, m. 70° (from EtOH).³¹⁶

254 PHOSPHATES, HALOPHOSPHATES, AND THIO ANALOGS

- (MeCH₂·CHMe·CH₂O)₂POSH.** Potassium salt: XXI. Needles (from CHCl₃-Et₂O).³²³
- (MeCH₂·CHMe·CH₂O)₂POSeH.** Potassium salt: XXI. Needles (from CHCl₃-Et₂O).³²³
- (*n*-C₁₆H₃₃O)₂PO(OH).** III.⁴⁰⁹ XVI.⁴⁰⁹ XVIIA.⁴⁰⁹ Obtained only in crude state; crystals, sinter at 64°. Barium salt, crystals (from dil. EtOH). Sodium salt.⁴⁰⁹
- (EtO)(PhCH₂O)PO(OH).** XVI. Sirup. Barium salt, crystals, soluble in water but insoluble in ethanol.³²³
- (iso-AmO)(PhCH₂O)PO(OH).** XIII-XVIIB (from iso-AmOH; partial dealkylation used).⁴² Silver salt, needles (from water).⁴²
- (PhCH₂O)₂PO(OH).** I.³⁴¹ III.^{41, 42} XVIIA.^{103, 339} Crystals, m. 79.5°,¹⁰³ m. 78-9° (from Et₂O),^{43, 339} m. 79-80°.⁴¹ Silver salt, crystals (from water), dec. 216°.^{42, 341} Barium salt, crystals (from water), dec. 255-61°.³⁴¹
- (EtHgO)₂PO(OH).** From trisilver phosphate and ethylmercury halide. From Et₄Pb, 90% phosphoric acid, and HgO in EtOH.⁷ Crystals, m. 176° (from EtOH).⁷

2. HALOGENATED DERIVATIVES

- (EtO)(ClCH₂CH₂O)PO(OH).** XVI. Barium salt.³²³
- (CH₂:CH·CH₂O)(ClCH₂CH₂O)PO(OH).** V-XVI. Barium salt, crystals (from EtOH).³²³
- (F₂CH·CH₂O)₂PO(OH).** XVIIA. Ammonium salt, plates (from EtOH-Et₂O). Barium salt, crystals (from dil. EtOH).⁴⁶⁰
- (ClCH₂·CHCl·CH₂O)₂PO(OH).** III. Calcium salt (dihydrate), needles, m. 273°.³⁰⁸
- (Br·CH₂·CHBr·CH₂O)₂PO(OH).** III. Needles. Calcium salt (4H₂O), needles, dec. 250°.³⁰⁸
- ((ClCH₂)₂CHO)₂PO(OH).** III. Calcium salt (4H₂O), needles, dec. 249°.³⁰⁸
- (Cl₃C·CHMeO)₂PO(OH).** III. Viscous mass.²⁶¹
- ((ClCH₂)₂C(NO₂)CH₂O)₂PO(OH).** XX. Amorphous, thermally unstable solid.³¹⁰
- ((BrCH₂)₂C(NO₂)CH₂O)₂PO(OH).** XX. Amorphous solid.³¹⁰
- (ICH₂)₂C(CH₂O)₂PO(OH).** III. Crystals, m. 102-3°. Calcium salt.¹⁹⁹
- (ClCH₂CH₂O)(*n*-C₁₆H₃₃O)PO(OH).** III.^{164, 261} Colorless needles, m. 54.5° (from Me₂CO).¹⁶⁴ Barium salt.¹⁶⁴

3. HYDROXY COMPOUNDS AND SIMPLE DERIVATIVES

- (MeO)(HOCH₂CH₂O)PO(OH).** V (from disodium glycol phosphate and dimethyl sulfate).⁸⁵ Calcium salt, crystals (from dil. EtOH).⁸⁵
- (MeO)(MeOCH₂CH₂O)PO(OH).** XVIIA (from the dimethyl analog).⁸⁵ Sodium salt, crystals (from water).⁸⁵
- (HOCH₂CH₂O)₂PO(OH).** III (from ethylene chlorohydrin and POCl₃, followed by heating the product, crude chloroethyl analog, with aqueous suspension of lead oxide).⁴⁰⁹ XVIIA (from the trichloroethyl analog with aqueous lead oxide).⁴⁰⁹ Barium salt (2H₂O), crystals (from water).⁴⁰⁹
- (MeO)((HOCH₂)₂CHO)PO(OH).** V. Calcium salt, m. 255°.⁸⁵
- (HOCH₂·CHOH·CH₂O)₂PO(OH).** V (from epichlorohydrin; followed by hydrolysis of the intermediate glycidic phosphate).⁷⁶ VII (from acetone-glycerol).³³⁰ By permanganate treatment of diallyl phosphate.⁷⁶ Barium salt.³³⁰
- (HOCH₂·CHOH·CH₂O)(HOCH₂)₂CHO)PO(OH).** V (from epichlorohydrin and disodium 2-glycerophosphate in hot water). Sodium salt, crystals (from dil. EtOH).^{81, 88}

$((\text{HOCH}_2)_2\text{CHO})_2\text{PO}(\text{OH})$. II (crude).⁴⁶⁰ III (from glycerol-1,3-dichlorohydrin; followed by hydrolysis with hot calcium hydroxide suspension).⁴⁶⁷ Calcium salt ($13\text{H}_2\text{O}$), needles, m. $249-50^\circ$ (from water).⁴⁶⁷

$\text{HOCH}(\text{CH}_2\text{O})_2\text{PO}(\text{OH})$. By heating an aqueous solution of disodium salt of glycerol-1-chlorohydrin-3-phosphate.^{74, 76} By treatment of disodium allyl phosphate with bromine in aqueous solution, followed by evaporation.⁷⁵ The reactions may be regarded as variants of V. Sodium salt.^{74, 75, 76}

$(\text{ICH}_2 \cdot \text{CHOH} \cdot \text{CH}_2\text{O})_2\text{PO}(\text{OH})$. XII (from epi-iodohydrin).¹⁹⁹ Calcium salt.¹⁹⁹

$((\text{PhOCH}_2)_2\text{CHO})_2\text{PO}(\text{OH})$. III-VI. Needles, m. 105° (from AcOH).¹¹⁵

$((p\text{-MeC}_6\text{H}_4\text{OCH}_2)_2\text{CHO})_2\text{PO}(\text{OH})$. III-VI. Needles, m. 160° (from dil. AcOH).¹¹⁵

4. DERIVATIVES OF NITROGEN BASES

$(\text{H}_2\text{NCH}_2\text{CH}_2\text{O})(n\text{-C}_{16}\text{H}_{33}\text{O})\text{PO}(\text{OH})$. By heating the 2-chloroethyl compound with alcoholic ammonia at 110° . Crystals, dec. 226° (from EtOH).¹⁶⁴

$(\text{HOCH}_2 \cdot \text{CHOH} \cdot \text{CH}_2\text{O})(\text{HOMe}_3\text{NCH}_2\text{CH}_2\text{O})\text{PO}(\text{OH})$. IV (using phenyl chlorophosphate).⁶⁵ Liquid, $[\alpha]_{\text{D}}^{25} -2.85^\circ$ (in water) for the active L-isomer; D,L-isomer prepared similarly from the inactive glycerophosphate.⁶⁵ Reineckate of the acetone derivative of the intermediate phenyl ester, m. $136-7^\circ$.⁶⁵

$(\text{HOMe}_3\text{NCH}_2\text{CH}_2\text{O})(\text{HOCH}_2)_2\text{CHO}\text{PO}(\text{OH})$. V.^{38, 424} Needles, m. $104-5^\circ$ (from EtOH-Et₂O).³⁸

$(\text{HOMe}_3\text{NCH}_2\text{CH}_2\text{O})_2\text{PO}(\text{OH})$. Isolated as the dibromide, by XVI.¹ Plates, m. 125° , dec. 166° .¹

Di-(uridine-2)-phosphate. IV (from 3',5'-benzylidene-uridine and phenyl dichlorophosphate),²⁵⁷ followed by XVIIA (XVIIIB does not appear to be effective). Barium salt, dec. $249-52^\circ$.²⁵⁷

4A. LECITHINS

$(\text{C}_{16}\text{H}_{31}\text{CO} \cdot \text{OCH}_2 \cdot \text{CHOH} \cdot \text{CH}_2\text{O})(\text{HOMe}_3\text{NCH}_2\text{CH}_2\text{O})\text{PO}(\text{OH})$. V. Crystals, dec. 262° .²⁹³

$((\text{C}_{16}\text{H}_{31}\text{CO} \cdot \text{OCH}_2)_2\text{CHO})(\text{HOMe}_3\text{NCH}_2\text{CH}_2\text{O})\text{PO}(\text{OH})$. From choline glycerophosphate and the acyl chloride in pyridine. Crystals, m. 160° , dec. 185° (from Me₂CO).²⁸⁹

$(\text{C}_{17}\text{H}_{35}\text{CO} \cdot \text{OCH}_2 \cdot \text{CH}(\text{O} \cdot \text{COC}_{17}\text{H}_{35}) \cdot \text{CH}_2\text{O})(\text{HOMe}_3\text{NCH}_2\text{CH}_2\text{O})\text{PO}(\text{OH})$. I (stepwise); (the synthesis does not preclude group migration). Plates or needles, m. 187° , dec. 190° (from MeOH or EtOH).²⁵³

$((\text{C}_{17}\text{H}_{35}\text{CO} \cdot \text{OCH}_2)_2\text{CHO})(\text{HOMe}_3\text{NCH}_2\text{CH}_2\text{O})\text{PO}(\text{OH})$. I (stepwise); the above remark applies in this case. Needles or plates, m. 195° , dec. 198° (from benzene).²⁵³

4B. CEPHALINS

$((\text{C}_{13}\text{H}_{27}\text{CO} \cdot \text{OCH}_2)_2\text{CHO})(\text{H}_2\text{NCH}_2\text{CH}_2\text{O})\text{PO}(\text{OH})$. VII (from myristin)-XIII (using hydroxyethylphthalimide, followed by cleavage with hydrazine). Crystals, m. $173-4^\circ$ (from EtOH).²⁷⁴

$((\text{C}_{16}\text{H}_{31}\text{CO} \cdot \text{OCH}_2)_2\text{CHO})(\text{H}_2\text{NCH}_2\text{CH}_2\text{O})\text{PO}(\text{OH})$. V. Crystals, m. 77° .²⁹³ The lecithin obtained from this substance, m. 81° .²⁹³ A more elegant synthesis, which insures the structure: VI (from palmitin)-XIII (best with hydroxyethylphthalimide, although carbobenzoxyethanolamine may be used). The intermediate carbobenzoxy derivative, m. $39.5-40^\circ$ (from Et₂O); the phthalyl derivative, m. $71-2^\circ$ (from ligroin). The free cephalin, m. $193-4^\circ$ (from EtOH).⁴²³ The intermediate dipalmito-2-glycerophosphate was also isolated; crystals, m. $102-4^\circ$ (from CHCl₃-ligroin); its 2-hydroxyethyl ester, obtained from the cephalin on treatment with nitrous acid, m. $49-51^\circ$ (from ligroin).⁴²³

256 PHOSPHATES, HALOPHOSPHATES, AND THIO ANALOGS

1-Stearo-3-eruco-2-cephalin. VII (from erucostearin)-XIII (using hydroxyethylphthalimide). Crystals, m. 163.5–64° (from EtOH).²⁷⁴

((C₁₇H₃₅CO·OCH₂)₂CHO)(H₂NCH₂CH₂O)PO(OH). By acylation of the glycerophosphate, followed by V. Crystals, m. 175°. ²⁹³

5. DERIVATIVES OF ACIDS

Di-isopyromucyl phosphate. XVIIA. Crystals, m. 154° (from EtOAc).¹⁶⁸

STRUCTURE UNCERTAIN

(*o*-MeC₆H₄NHCO·CH₂O)₂PO(OH). XX. Amorphous, m. 168–70° (from CHCl₃).¹¹¹

(*p*-MeC₆H₄NHCO·CH₂O)₂PO(OH). XX. Solid, m. 255–7°. ¹¹¹

B. COMPOUNDS WITH THE ESTER LINKAGE TO A CYCLIC STRUCTURE

1. HYDROCARBON DERIVATIVES

(MeO)(PhO)PS(SH). XXII. Nickel salt, m. 113–4°. ³⁴⁹

(EtO)(PhO)PO(OH). III. Sirup. Barium salt, crystalline powder (from EtOH).

Lead salt, powder. Sodium salt, crystals (from water). ³⁶⁸

(PhO)₂PO(OH). I. ⁴²⁸ III. ^{105, 265, 287, 421} X. ⁴⁷ XVI. ⁴⁰⁹ XVIIA. ²⁴⁷ Plates, m. 61–2°, ⁴⁷ m. 56° (impure), ⁴²¹ represent partial hydrates; pure dihydrate forms plates, m. 51° (from water), whereas the anhydrous ester forms needles, m. 70° (from CHCl₃-ligroin). ²⁶⁵ Ammonium salt, m. 130°. Sodium salt (5H₂O), plates, m. 70°. Silver salt, needles, m. 213°. Barium salt (4H₂O), needles (from dil. EtOH).

(PhO)₂POSH. III. ^{51, 375, 402} X. ⁵¹ XVIIA. ^{51, 402} XVIII. ⁴⁰² Poorly stable oil. Sodium salt: plates (from dil. EtOH). ⁵¹ It is claimed that the (O)-salt forms from the chlorothionophosphate (III), in the form of water-soluble needles, whereas methanolic sodium methoxide and the tertiary thionophosphate (XVIIA) interaction results in the (S)-salt, which is insoluble in water. ⁴⁰² Lead salt: it is claimed that the above forms of sodium salt give, with lead acetate, two forms of the lead salt, respectively: (O)-salt, prisms, m. 112° (from EtOH), and (S)-salt, oily and amorphous, soluble in ether. ⁴⁰² This information lacks recent confirmation. Silver salt: claimed to be the (S)-salt (by XVIII), prisms, dec. 300° (from EtOH). ⁴⁰²

(PhO)₂PS(SH). XXII. ^{132, 349} Crystals, m. 61°. ¹³² Nickel salt, m. 130°. ³⁴⁹ The acid yields a pyro derivative at 150°. ¹³²

(PhO)(4-MeC₆H₄O)PO(OH). III. Needles, m. 54° (from benzene-ligroin). ³⁴⁰

(2-MeC₆H₄O)₂PS(SH). XXII. Nickel salt, m. 124°. ³⁴⁹

(4-MeC₆H₄O)₂PS(SH). XXII. ³⁴⁹ XVI. ⁴³⁵ Nickel salt, blue-violet, m. 175, ³⁴⁹ m. 174–5°. ⁴³⁵

(2-iso-Pr-5-MeC₆H₃O)₂PO(OH). III. XVIIA. Solid. ¹⁸⁹ Barium salt, needles. ¹⁸⁹ Sodium salt, needles. ³¹⁸

(2-Me-4-BuC₆H₃O)₂PO(OH). III. Potassium salt. ⁴³⁴

(2-Me-4-iso-AmC₆H₃O)₂PO(OH). III. Potassium salt. ⁴³⁴

(2-Me-4-C₆H₁₃·C₆H₅O)₂PO(OH). III. Potassium salt. ⁴³⁴

(2-iso-Pr-5-Me-6-Bu·C₆H₂O)₂PO(OH). III. Potassium salt. ⁴³⁴

Dimethyl phosphate. XI (from levo isomer of ROH). Crystals, m. 105°. ³⁶² Sodium salt. Silver salt. Lead salt, solid, may be also obtained by heating an alleged pyrophosphate (R₂P₂O₇H₂) with lead nitrate. ³⁶²

(PhO)(2-C₁₀H₇O)PO(OH). III. Needles, m. 92–3°. ³⁰⁹

(2-C₁₀H₇O)₂PO(OH). III. ³²¹ X-III. ⁴⁷ XVIIA. ⁴⁷ Prisms (from CHCl₃), m. 147–8°, ⁴⁷ m. 142°. ³²¹ Sodium salt, plates (from water). Phenylhydrazine salt, m. 183°. ⁴⁷

1-(2,4-Ph₂-C₁₀H₅O)₂PO(OH). XVIIA. Crystals, m. 220–1°. ³²⁶

2,2'-(1,1'-dinaphthylene) phosphate. III. Needles. Sodium salt.⁸⁵⁰

Dicholesteryl phosphate. VI-III.^{211, 212, 409} XIII (using N,N-diphenylamido-dichlorophosphate).⁵⁰⁵ Crystals, m. 204° (from benzene-EtOH), m. 208°,⁵⁰⁵ m. 186°.²¹¹ Barium salt, crystals (from EtOH).⁴⁰⁹ It is claimed that the anhydrous free ester is in reality highly associated and may be regarded as a pyrophosphate because it is insoluble in dilute alkali and fails to react with sodium in warm toluene.^{481, 505}

(O,S)-Dicholesteryl thiophosphate. (RO)(RS)PO(OH). Claimed to be obtained by XXII. Crystals, m. 188°, insoluble in aqueous alkali.⁴⁸¹

(S,S)-Dicholesteryl dithiophosphate. (RS)₂PO(OH). The identity and the existence of this compound is controversial. The product obtained by XXII (excess P₂S₅), m. 188-9°, is insoluble in aqueous alkali and poorly soluble in ether.⁴⁸¹ The reaction in which 4 moles of cholesterol are used allegedly forms the ortho derivative, (RS)₂P(OH)₃, isolated as a disodium salt, dec. 266°, by heating the product with sodium in toluene; its piperidine salt, m. 220-2°. However, thiocholesterol and phosphorus oxychloride in pyridine (VI) yield a product, m. 180-3°, that is soluble in ether and regarded as a (S)ester of pyrophosphoric acid, which gives a tetrasodium salt with sodium ethoxide. The salt, m. 285°, is regarded as a salt of an ortho derivative, formulated as (RS)₂P(ONa)₂O-P(ONa)₂(SR)₂. Regeneration of the free ester from this salt yields a product, m. 170-1°.⁴⁸¹

Diergosteryl phosphate. VI-III. Crystals (from pyridine).²¹²

2. SUBSTITUTED DERIVATIVES

(2-ClC₆H₄O)₂PO(OH). III.^{118, 509} Needles, m. 121.5°,¹¹⁸ m. 105-6°.⁵⁰⁹

(4-ClC₆H₄O)₂PO(OH). III.^{434, 509} X.⁴⁷ XVIIA.⁴⁷ Needles or plates, m. 133-5°.⁵⁰⁹ m. 126-7°.⁴⁷ Sodium salt, poorly soluble in cold water.⁴⁷ Ferric salt, very insoluble in water.⁵⁰⁹

(4-BrC₆H₄O)₂PO(OH). By bromination of diphenyl phosphate in hot CHCl₃. Needles, m. 199-201° (from water or CHCl₃).⁵⁰⁹

(2,4,6-Cl₃C₆H₂O)₂PO(OH). III. Crystals, m. 238°.¹¹⁸ Somewhat less pure preparations are: III (m. 201°)¹¹⁸ and modified XX, in which trichlorophenol is heated with PCl₃, then with PCl₅ at 200-300°, followed by III;⁵⁰¹ the latter product, m. 230° (from dil. EtOH). Barium salt, needles. Ammonium salt, solid, poorly soluble in water.⁵⁰¹

(3-Me-4-ClC₆H₃O)₂PO(OH). III. Crystals, m. 116°.⁴³⁴

(2,4,6-Cl₃-3-MeC₆H₂O)₂PO(OH). XX. Needles, m. 94.5° (from dil. EtOH).¹²⁸

(2-Me-5-iso-Pr-6-ClC₆H₂O)₂PO(OH). III. Solid.⁴³⁴

(2-iso-Pr-5-Me-6-ClC₆H₂O)₂PO(OH). III. Crystals, m. 134°.⁴³⁴

2-(1-ClC₁₀H₆O)₂PO(OH). X. Needles, m. 251° (from EtOH).⁴⁷

(4-O₂NC₆H₄O)₂PO(OH). By nitration of diphenyl phosphate with nitric acid (d. 1.5).²⁶⁵ By nitration of diphenyl amidophosphate at 0°.²⁰⁹ Nitration in the presence of alcohol or treatment of the nitration mixture with alcohol yields not the above compound as claimed by Rapp (m. 133.5°)⁴²¹ but its ethyl ester. The authentic compound, m. 175° (from EtOAc),²⁶⁵ forms a poorly soluble sodium salt, plates (from water), and a silver salt, needles (from hot water).²⁶⁵

(2-MeOC₆H₄O)₂PO(OH). I.¹⁹⁶ III.⁴⁶ VI-III.⁴⁶ XVIIA.⁴⁶ Prisms, m. 97° (from water).^{46, 196} Sodium salt. Copper salt, needles, soluble in water. Calcium salt, needles, soluble in water.⁴⁶ Potassium salt.¹⁹⁶

(2-Me-4-PrCO·C₆H₃O)₂PO(OH). III. Potassium salt.⁴³⁴

(2-iso-Pr-5-Me-6-PrCO·C₆H₃O)₂PO(OH). III. Potassium salt.⁴³⁴

(4-HO₃S-2-HO₂CC₆H₃O)₂PO(OH). From 5-sulfosalicylic acid and sodium phosphate in hot aqueous solution. Prisms (dihydrate),⁸⁴ isolated as the trisodium salt.

3,4-Tetrahydrofurylene-phosphate (presumably cyclic). II (from phosphoric acid and erythritol at 110–25° in vacuo).¹³⁵ By heating 4-hydroxy-tetrahydrofuryl phosphate.¹³⁵ Prisms, dec. 205°.¹³⁵ The identity of this substance is not completely certain.

III. TERTIARY ESTERS

A. COMPOUNDS WITH THE ESTER LINKAGE TO AN ALIPHATIC CARBON

1. HYDROCARBON DERIVATIVES

(MeO)₃PO. V.^{151, 339, 418, 464} X.^{192, 213, 290, 475} XV.¹⁵¹ As by-product, from sodium methoxide and PCl₃.^{31, 32} Liquid, b. 197.2°,⁴⁸⁴ b. 192–3°,^{31, 32} b₇₆₂ 192°,¹⁵¹ b₆₀ 110°,¹⁵¹ b₃₆ 97°,¹⁵¹ b₂₄ 85°,¹⁵¹ b₁₂ 79°,³⁸⁰ b₁₀ 73°,²¹³ b₈₋₁₀ 72–3°,³¹ b₆₋₇ 67–8°,³⁹⁰ b₅ 62°;⁴⁷⁵ d₀^{1.2365},¹⁵¹ d₀^{1.2156},^{31, 32} d₀^{1.2148},³¹ d₀^{1.218},¹⁹² d₀^{1.2195},¹⁵¹ d₀^{1.1971},^{31, 32} d₄²⁰ 1.2144,⁴⁷⁵ d₄²² 1.200,⁴¹⁸ d₄²⁵ 1.2052,²¹³ d₄^{60.9} 1.1722, d₄^{119.9} 1.1062;⁴⁷⁵ n_D²⁰ 1.39452,⁴⁷⁵ n_D²⁰ 1.39630, n_F²⁰ 1.40049,⁴⁷⁵ n_C²⁵ 1.3934, n_D²⁵ 1.3950, n_F²⁵ 1.3990.²¹³ Solubility in water: 1:1 at 25°.¹⁹²

(MeO)₂(MeS)PO. V.^{202, 400} XVIII.⁴⁰² Liquid, b₁₂ 103°,⁴⁰⁰ b₂₀ 107°,⁴⁰² b₃ 99–100°,⁴⁰² d₀^{1.2685},^{400, 402} n_D¹⁰ 1.46864.²⁰²

(MeO)₂(MeSe)PO. Isolated as the mercuric iodide salt (yellow, infusible plates) by XVIII (from (RO)₃PSe and mercuric iodide).⁴⁰²

(MeO)₃PS. X.^{400, 402} Liquid, b₂₀ 82°,^{400, 402} b₁₂ 78°,^{400, 402} b₁₂ 80°,²⁰² b₃ 75°;²⁰² dec. 116°;⁴⁰² d₀^{1.2192},^{400, 402} d₀^{1.2053},²⁰² n_D^{10.5} 1.4583.²⁰² Luminesces in air.¹⁸⁵ Double salts: 2HgI₂, dec. 102° (from EtOH),⁴⁰² 2FeCl₃, m. 125°, dec. 131° (from MeOH-Et₂O),⁴⁰² 2FeBr₃, m. 99° (from ligroin),⁴⁰² AuCl₃, m. 110°.⁴⁰²

(MeO)₃PSe. XXI. Liquid, b₂₀ 95°, d₀^{1.5387},⁴⁰² HgI₂ salt, m. 66°.⁴⁰²

(MeO)₂(MeS)PS. XXII (besides dimethyl dithiophosphate).^{185, 216} Liquid, b₁₄ 103°, d₀^{1.2587}, d₄¹⁷ 1.2427.¹⁸⁵

(MeO)₂(EtO)PO. V.^{192, 339, 484} Liquid, b. 203.3°,^{339, 484} b. 203°,¹⁹² d₀^{1.176},¹⁹² d₀^{1.1752},^{339, 484} d₀²² 1.161.¹⁹² Solubility in water: 1:1 at 25°.

(MeO)(EtO)₂PO. V.³³⁹ Liquid, b. 208.2°, d₀^{1.1228}.³³⁹

(EtO)₃PO. V.^{151, 339} VI.¹⁹⁸ X.^{136, 147, 192, 213, 386, 475} XI.⁴⁸⁸ XV.⁴⁷⁴ XVI.³²⁵ XXIII.⁴⁰² Liquid, b₇₇₀ 216°,⁸⁴ b₇₇₅ 211.5°(?),¹⁵¹ b₇₆₀ 215–6°,³¹ b₇₆₀ 215°,¹⁹² b₇₄₅ 214°,⁸⁴ b. 203° (in H atm.?),⁴⁸⁸ b₅₀ 123°,¹⁵¹ b₃₀ 116°,¹⁴⁷ b₂₅ 108°,³⁴ b₂₅ 103°,¹⁵¹ b₁₃ 99.2°,³⁴ b₁₀ 90°,²¹³ b₈₋₁₀ 98–8.5°,¹⁵¹ b₅ 75.5°,⁴⁷⁵ b₂ 77–9°,³³ d₀^{1.0929},¹⁵¹ d₀^{1.0897},²³ d₀^{1.0897},^{31, 32} d₀^{12.5} 1.0785,¹⁵¹ d₀¹⁹ 1.0725,³¹ d₀²⁰ 1.06817,³⁴ d₄²⁰ 1.0695,⁴⁷⁵ d₄²² 1.056(?),¹⁹² d₄²⁵ 1.0637,²¹³ d₀⁵⁵ 1.0214,¹⁵¹ d₀^{60.9} 1.0301,⁴⁷⁵ d₄^{120.1} 0.9708,⁴⁷⁵ n_D²⁰ 1.4063,³³ n_D²⁰ 1.40533,⁴⁷⁵ n_D²⁰ 1.40616,³⁴ n_D¹⁷ 1.40674,⁵⁰⁴ n_D²⁵ 1.4039,²¹³ n_C²⁰ 1.40343, n_F²⁰ 1.40983,⁴⁷⁵ n_C²⁵ 1.4021, n_F²⁵ 1.4082.²¹³ Solubility in water: 1:1 at 25°.¹⁹²

(EtO)₂(EtS)PO. XVIII.⁴⁰² XVIII–V.^{400, 402} Liquid, b₂₀ 122°,⁴⁰² b₁₆ 120°,⁴⁰⁰ b. 237° (slight decomposition),⁴⁰² d₀^{1.1245}.⁴⁰²

(EtO)₂(EtSe)PO. V. XVIII.⁴⁰² Liquid, b₂₀ 140°, d₀^{1.3593},⁴⁰² double salt with HgI₂, m. 95°.⁴⁰²

(EtO)(EtS)₂PO. V. X. XVIII. Liquid, b₂₀ 148°, d₀^{1.1623}.⁴⁰²

(EtS)₃PO. V.⁴⁰² X.^{155, 402} XIV.³³⁸ XVIII.⁴⁰² Liquid, b₂₀ 174–5°,^{155, 402} b₁₆ 172–4°,¹⁵⁵ b₁₅ 165–8°,³⁸⁸ m. –24°,³⁸⁸ d₀^{1.1968},⁴⁰² d₄²⁵ 1.1890.³³⁸

(EtO)₃PS. V.^{400, 402} X.^{156, 382, 400, 402} XI(?).^{184, 355} XXI.^{37, 402, 467} Liquid, b₇₄₅ 216°,⁴⁰² b₂₀ 106°,^{400, 402} b₂₀ 105–6°,³⁵² b₁₆ 100°,⁴⁰⁰ b₁₂ 95°,⁴⁵⁷ b₈ 88.5°,³⁷ d₀^{1.0944},⁴⁰² d₄²⁰ 1.1132(?),⁴⁵⁷ d₀²⁰ 1.0756,³⁷ n_D²⁰ 1.4480.³⁷ Stable to distillation with steam.⁴⁰² Oxidizes in air with luminescence.¹⁸⁵ Double salts: 2PtCl₄, m. 103°; 2HgI₂, m. 88°.⁴⁶⁸

Treatment with sulfuric acid is claimed to transform this ester into tetraethyl dithiopyrophosphate.¹³⁴

(EtO)₃PSe. XXI. Liquid, b_{20} 117°, d_4^{20} 1.3189,⁴⁰² Salt with HgI₂, m. 32°.⁴⁰²

(EtO)₂(EtS)PS. V.^{401, 402} X.⁴⁰² XXII.^{133, 401, 402} Liquid, b_{20} 128°, d_4^{20} 1.1341.⁴⁰² Salt with 2HgI₂, m. 86°.⁴⁰²

(EtO)(EtS)₂PS. X. Liquid, b_{20} 155°, d_4^{20} 1.1716.⁴⁰² Salts: 2HgCl₂, m. 81°; 2HgI₂, m. 112°.⁴⁰²

(EtO)₂(EtSe)PSe (probably). XXII. Oil.¹³⁵

(EtS)₃PS. X. XXII (using EtSH).^{133, 402} Liquid, b_{20} 182°, d_4^{20} 1.2229.⁴⁰² Salt with 2HgCl₂, m. 84° (from MeOH).⁴⁰²

(MeO)₂(PrO)PO. V. Liquid, b_{15} 116°, d_4^{20} 1.195, d_4^{22} 1.180.¹⁹²

(MeO)(PrO)₂PO. V. Liquid, b_{20} 129°, d_4^{20} 1.077, d_4^{22} 1.059.¹⁹²

(EtO)₂(PrO)PO. V. Liquid, b_{20} 130°, d_4^{20} 1.098, d_4^{22} 1.077.¹⁹²

(EtO)(PrO)₂PO. V. Liquid, b_{20} 145°, d_4^{20} 1.046, d_4^{22} 1.025.¹⁹²

(PrO)₃PO. V.¹⁵² VI.¹⁹⁸ X.^{192, 213, 475} XI.⁴⁷¹ XX.⁴⁹¹ As a by-product from RONA and PCl₃ reaction.^{31, 32} Liquid, b_{47} 138°, b_{22} 133°,¹⁵² b_{15} 131°,¹⁹² b_{15} 128–34°,¹⁹⁸ b_{10} 121°,²¹³ b_9 119°,⁴⁷¹ b_{8-10} 120.5–1.5°,³¹ b_8 120–1°,³² b_5 107.5°,⁴⁷⁵ d_4^{20} 1.025,¹⁹² d_4^{20} 1.0282,³¹ d_4^{20} 1.0121,⁴⁷⁵ d_4^{22} 1.007,¹⁹² d_4^{25} 1.0023,²¹³ $d_4^{120.7}$ 0.9209,⁴⁷⁵ n_D^{20} 1.41646,⁴⁷⁵ n_D^{25} 1.4136,²¹³ n_C^{20} 1.4148,⁴⁷⁵ n_C^{25} 1.4118,²¹³ n_F^{20} 1.42120,⁴⁷⁵ n_F^{25} 1.4182.²¹³

(PrO)₂(PrS)PO. V. XVIII.⁴⁰² Liquid, b_{20} 156°, d_4^{20} 1.0532.⁴⁰²

(PrO)₃PS. X. Liquid, b_{20} 133–4°, d_4^{20} 1.0409; salt with 2HgCl₂: oil.⁴⁰²

(CH₂:CH·CH₂O)₃PO. VI.⁴⁸⁷ V.¹⁵¹ Liquid, $b_{0.5}$ 80°,⁴⁸⁷ b_{44} 157°, b_{20} 142°.¹⁵¹

(iso-PrO)₃PO. V.¹⁵² X.⁴⁷⁵ By-product in the reaction of RONA with phosphorus trichloride.^{31, 32} Liquid, b 218–20°,³² b_{68} 136°,¹⁵² b_{8-10} 95–6°,^{31, 32} b_5 83.5°,⁴⁷⁵ d_4^{20} 1.0054,^{31, 32} d_4^{20} 0.9867,⁴⁷⁵ $d_4^{62.5}$ 0.9472,⁴⁷⁵ $d_4^{119.9}$ 0.8931,⁴⁷⁵ n_C^{20} 1.40376,⁴⁷⁵ n_D^{20} 1.40573,⁴⁷⁵ n_F^{20} 1.41034.⁴⁷⁵

(EtO)₂(BuO)PO. XIII.²⁴¹ VIII.⁴³⁸ Liquid, b_{15} 123°,²⁴¹ b_{3-4} 82–7°,⁴³⁸ d_4^{10} 1.0380,⁴³⁸ d_4^{13} 1.0340,²⁴¹ d_4^{25} 1.0243,⁴⁷⁵ n_D^{10} 1.4170,⁴⁷⁵ n_D^{20} 1.4131.⁴³⁸

(EtO)(BuO)₂PO. VIII. Liquid, b_{3-4} 95–6°, d_4^{10} 1.0112, d_4^{25} 0.9984, n_D^{10} 1.4215, n_D^{20} 1.4182.⁴³⁸

(BuO)₃PO. VI.^{198, 241} VI (using PCl₅).²⁴¹ X.^{37, 213, 475} XI.^{375, 471} XIII.²⁴¹ XIV.¹²⁶ Liquid, b_{20} 180°, b_{15} 160–2°, b_{10} 154°,²⁴¹ b_{10} 150°,²¹³ b_8 143–5°,¹⁹⁸ b_8 148.5°,³⁷ b_6 138.5°,⁴⁷⁵ b_5 135°,³⁷⁵ d_4^{13} 0.9824,²⁴¹ d_4^{20} 0.9731,³⁷ d_4^{20} 0.9766,⁴⁷⁵ d_4^{25} 0.9727,²¹³ $d_4^{120.5}$ 0.8941,⁴⁷⁵ n_C^{20} 1.42295,⁴⁷⁵ n_D^{20} 1.42496,⁴⁷⁵ n_D^{20} 1.4247,³⁷ n_F^{20} 1.42988,²⁴¹ n_C^{25} 1.4203, n_D^{25} 1.4224, n_F^{25} 1.4274.²¹³

(MeEtCHO)₃PO. VI. Liquid, b_{8-12} 119–29°.¹⁹⁸

(EtO)₂(iso-BuS)PO. V. XVIII.⁴⁰² Liquid, b_{20} 138°, d_4^{20} 1.0899.⁴⁰²

(iso-BuO)₃PO. V.¹⁵² X.^{192, 213, 475} XI.³⁷⁵ By-product of the reaction of RONA and phosphorus trichloride.^{31, 32} Liquid, b_{15} 152°,¹⁹² b_{10} 135–6°,³¹ b_{10} 138°,²¹³ $b_{5.5}$ 117°,⁴⁷⁵ b_4 112°,³⁷⁵ d_4^{20} 0.9698,^{31, 32} d_4^{20} 0.9681,⁴⁷⁵ d_4^{25} 0.9617,²¹³ $d_4^{120.8}$ 0.8818,⁴⁷⁵ n_C^{20} 1.41729,⁴⁷⁵ n_D^{20} 1.41931,⁴⁷⁵ n_F^{20} 1.42416,⁴⁷⁵ n_C^{25} 1.4152, n_D^{25} 1.4173.²¹³

(iso-BuO)₂(iso-BuS)PO. V. XVIII. Liquid, b_{20} 170°, d_4^{20} 1.0101.⁴⁰²

(iso-BuO)₃PS. X. Liquid, b_{20} 155°, d_4^{20} 0.9907.⁴⁰²

(CH₂:CMe·CH₂O)₃PO. X. Liquid, b_5 134.5–40°, d_4^{26} 0.988, n_D^{25} 1.4454.³⁶⁰

(CH₂:CMe·CH₂O)₂(EtO)PO. Crude. X. Liquid, b_6 120–35°, n_D^{25} 1.4390.³⁶⁰

(AmO)₃PO. VI.¹⁹⁸ X.^{213, 475} XI.³⁷⁵ Liquid, b_{50} 225°,²¹³ b_6 158–63°,¹⁹⁸ b_5 167°,⁴⁷⁵ $b_{2.5}$ 143–4°,³⁷⁵ d_4^{20} 0.9608,⁴⁷⁵ d_4^{25} 0.9497,²¹³ $d_4^{120.6}$ 0.8816,⁴⁷⁵ n_C^{20} 1.42975, n_D^{20} 1.43188, n_F^{20} 1.43701,⁴⁷⁵ n_C^{25} 1.4262, n_D^{25} 1.4283, n_F^{25} 1.4332.²¹³

(BuO)(iso-AmO)₂PO. XIII. Liquid, $b_{4.5}$ 145°.³⁷⁵

(iso-AmO)₃PO. V.³⁶⁸ XI.⁴⁷¹ Liquid, b_8 143°.⁴⁷¹

(iso-AmO)₃PS. X. Liquid, d_4^{12} 0.849; can be steam-distilled.¹⁸³

(iso-AmS)₃PS. By-product from XXII. Yellow oil, dec. 100°. ³¹⁶

(BuCEtH·CH₂O)₃PO. VI. Liquid, b_{3.5} 203°, d₂₀²⁰ 0.924. ¹⁴³

(n-C₁₂H₂₅O)₃PO(?). I. XX. Crystals, m. 61° (from ligroin). ⁴⁰⁹ The preparation has not been verified and is the sole example of a tertiary phosphate of one of the higher alcohols.

(EtO)₂(PhCH₂O)PO. XVI. Liquid, b₁₂ 150°. ³²⁵

(MeO)(PhCH₂O)₂PO. V. Liquid, d₀⁰ 1.2089. ³³⁹

(PhCH₂O)₃PO. V. Prisms, m. 65°, ¹¹⁸ m. 64°. ³³⁹

(PhCH₂S)₃PS. XXII. Liquid, m. -13° (from EtOH). ⁴³⁵

(Ph₂CHO)(PhCH₂O)₂PO. XXIV. Crystals, m. 72-2.5° (from ligroin). ⁴¹

(PhCO·CPhHO)(PhCH₂O)₂PO. XXIV. Crystals, m. 53-4°. ⁴¹

(EtHgO)₃PO. From Et₄Pb, HgO and 90% H₃PO₄ in hot EtOH. Crystals, m. 145° (from EtOH-EtOAc). ⁷

(Me₃SiO)₃PO. Modified I (from hexamethylsiloxane and P₂O₅). Liquid, b₄ 85-7°, n_D²⁰ 1.4090. ⁴⁴⁰

2. HALOGEN DERIVATIVES

(EtO)₂(FCH₂CH₂O)PO. XIII. Liquid, b₁₃ 123-4°. ⁴⁴²

(MeO)₂(ClCH₂CH₂O)PO. XIII. Liquid, b₄ 95-6°. ⁴²⁹

(EtO)₂(ClCH₂CH₂O)PO. XIII. Liquid, b₁₈ 144-5°, ⁴⁴² b_{4.5} 118-9°. ¹⁸³

(ClCH₂CH₂O)₃PO. XI. ²⁸⁸ XII. ²⁸⁰ Less satisfactory: XI, ^{291, 409} VI. ²⁹¹ Liquid, b₅ 180°, b₁₀ 194°, b₁₅ 202°, b₂₅²⁵ 214°, ²⁹¹ b₂₋₃ 180-2°, ²⁸⁸ b₄₀ 190° (apparently erroneous), ⁴⁰⁹ d₄²⁰ 1.4256, ²⁹¹ d₂₀²⁰ 1.428, ²⁸⁶ n_C²⁰ 1.4708, n_D²⁰ 1.4731, n_F²⁰ 1.4786. ²⁹¹

(F₂CHCH₂O)₃PO. From ROH, bromine, and red phosphorus. Oil, b. 253-5°. ⁴⁶⁰

(Cl₃C·CH₂O)₃PO. XX. Crystals, m. 73-4°; sublimable. ¹⁸⁴

((ClCH₂)₂CHO)₃PO. VI. Liquid, b₁₀ 246°, b₅ 236-7°, d₄²⁰ 1.5182, n_D²⁰ 1.5022, n_C²⁰ 1.4997, n_F²⁰ 1.5083. ²⁹¹

(ClCMeH·CCl₂·CH₂O)₃PO. XX. Needles, m. 85.3-5.4° (from EtOH). ³⁸⁷

3. DERIVATIVES WITH HYDROXY GROUPS (FREE AND SUBSTITUTED)

(MeO)₂(MeOCH₂CH₂O)PO. V. Liquid, b₉ 112-3°, d₄²⁰ 1.1820, n_D²⁰ 1.4140. ⁸⁵

(BuO)₂(EtOCH₂CH₂O)PO. XI (in two steps). Liquid, b₂₀ 200-250°. ²⁷⁸

(BuO)(ClCH₂CH₂O)(MeOCH₂CH₂O)PO. XIII. Liquid, b₁₃ 195-205°. ²⁷⁸

(ClCH₂CH₂O)₂(EtOCH₂CH₂O)PO. XI (in two steps). Liquid, n_D²⁰ 1.453. ²⁷⁸

(BrCH₂CH₂O)(MeOCH₂CH₂O)(BuOCH₂CH₂O)PO. XIII. Liquid, b₇ 205-10°. ²⁷⁸

(MeOCH₂CH₂O)₂(BuOCH₂CH₂O)PO. XI (in two steps). Liquid, b₂₀ 215-20°. ²⁷⁸

(MeOCH₂CH₂O)₂(PhOCH₂CH₂O)PO. XI (in two steps). Liquid, b₂₀ 225-35°. ²⁷⁸

(EtOCH₂CH₂O)₃PO. XI. Liquid, b₂₀ 225°. ²⁷⁸

(BuOCH₂CH₂O)₃PO. XI. Liquid, b₁₀ 255°. ²⁷⁸

(PhOCH₂CH₂O)₃PO. XI. Liquid, which crystallizes and m. 142°. ²⁷⁸

(BuOCH₂CH₂CH₂O)₃PO. XI. Liquid, b₁₀ 248°. ²⁷⁸

1,2,3-Glycerol phosphate. Alleged to be a monomolecular tricyclic ester; this structure appears to be highly improbable. II. Amorphous mass; generally insoluble. ¹⁸⁹

MeOCH₂CHCH₂OP(S)(OEt)O. XXI. Liquid, b₂ 121.5-22°, d₀²⁰ 1.2359, n_D²⁰ 1.4790. ⁸⁵

MeOCH₂CHCH₂OP(S)(OMe)O. XXI. Liquid, b_{1.5} 111-2.5°, d₀²⁰ 1.2877, n_D²⁰ 1.4889. ⁸⁵

(MeO)₂(MeOCH₂·CH(OMe)CH₂O)PO. V (from disilver glycerophosphate, methyl iodide, and silver oxide). Dextro form: liquid, *b*_{0.7} 122°, [*α*]_D 2.38° (in EtOH).^{205, 419}
 Levo form: liquid, *b*_{0.8} 125–6°, *b*_{0.4} 110–2°, [*α*]_D –3.28° (in EtOH).²⁰⁵
(MeO)₂((MeOCH₂)₂CHO)PO. V (as above). Liquid, *b*_{0.8} 126–8°. ²⁰⁸
(EtOCH₂CH(OEt)CH₂O)(EtO)₂PO. V (as above). Liquid, *b*_{0.13} 100–100.5°, *b*_{0.03} 92–3°, *n*_D¹⁹ 1.4260, [*α*]_D¹⁹ –5.76° (in EtOH). The product is the L-(–) isomer from the corresponding glycerophosphate. Its corresponding trimethyl analog, *b*_{0.13} 87–8°, [*α*]_D –4.78°. ⁶⁰

3A. CARBOHYDRATE DERIVATIVES

Methyl di-1-(1-chloro-*d*-galactosepenta-acetate) phosphate. XIII. Crystals, m. 187–8° (with decomposition).⁴⁹⁶
Ethyl di-1-(1-chloro-*d*-galactosepenta-acetate) phosphate. XIII. Crystals, m. 156–8°. ⁴⁹⁶
Dibenzyl 2,3,4,6-tetra-acetyl-*d*-glucose phosphate. V. Crystals, m. 79°. ⁵⁰⁶
Tri-(diacetoneglucose) phosphate. X. Solid, m. 55°. ³⁷⁷
Tri-(hepta-acetyl-maltose) phosphate. V. Crude solid. ³⁵³

4. CARBOXYLIC DERIVATIVES

(PhNHCO·CH₂O)₃PO. XI. XX. Needles, m. 196° (from EtOH).¹¹¹
(*o*-MeC₆H₄NHCO·CH₂O)₃PO. XX. Prisms, m. 143° (from EtOH).¹¹¹
(*p*-MeC₆H₄NHCO·CH₂O)₃PO. XX. Needles, m. 188° (from EtOH).¹¹¹
(2-C₁₀H₇NHCO·CH₂O)₃PO. XX. Needles, m. 192–6° (from EtOH).¹¹¹
(EtO₂C·CHMeO)₃PO. VI. Undistillable oil, *n*_D¹⁸ 1.4350, *d*₄²⁰ 1.200. ³⁴⁴
(PhNHCO·CHMeO)₃PO. XI–XX. Plates, m. 205° (from EtOH).¹¹¹
(*o*-MeC₆H₄NHCO·CHMeO)₃PO. XI–XX. Crystals, m. 177° (from EtOH).¹¹¹
(*p*-MeC₆H₄NHCO·CHMeO)₃PO. XI–XX. Crystals, m. 156° (from EtOH).¹¹¹
(PhNHCO·CMe₂O)₃PO. XI–XX. Plates, m. 158–9° (from EtOH).¹¹¹
(*o*-MeC₆H₄NHCO·CMe₂O)₃PO. XX. Needles, m. 194–6° (from EtOH).¹¹¹
(*p*-MeC₆H₄NHCO·CMe₂O)₃PO. XX. Needles, m. 160–2° (from dil. AcOH).¹¹¹
(EtO)₂(EtO₂C·CH:CMeO)PO. X. Liquid, *b*₂ 138°. ¹⁰⁹
(EtO)₂(EtO₂C·CH:CMeO)PO. Liquid, *b*₁₂ 139°. ¹⁰⁹
(EtO)₂(EtO₂C·CH:CMeO)PS. Liquid, *b*₅ 154°. ¹⁰⁹
Tri-isopyromucyl phosphate. X. XX. Prisms, m. 138° (from EtOAc).¹⁵⁸

5. NITROGENOUS DERIVATIVES

(MeO)₂(ClMe₃NCH₂CH₂O)PO. From the 2-chloroethyl analog and trimethylamine in toluene. Hygroscopic needles, m. 136.5–37°. ⁴²⁹
(ClMe₃NCH₂CH₂O)₃PO. As above, from tri-2-chloroethyl analog. Solid, dec. 245° (from EtOH). Chloroaurate, needles, m. 216°. ²⁸⁶
(Me₂C(NO₂)·CH₂O)₃PO. XI–XX. Crystals, m. 155° (from BuOH). ⁴⁷⁰
(MeEtC(NO₂)·CH₂O)₃PO. XI–XX. Undistillable solid, m. 23–5°. ⁴⁷⁰
O₂NC(CH₂O)₃PO. VI. Prisms, m. 243° (from water).⁵¹⁰ The structure of this substance does not appear to be probable.

B. COMPOUNDS WITH ESTER LINKAGE TO A CYCLIC STRUCTURE

1. DERIVATIVES OF CYCLIC HYDROCARBONS

(EtO)₂(PhO)PO. VIII. ³⁶⁷ X. ^{366, 365} Liquid, *b*₇₀ 200–30°, *b*₁₈ 146–62°; ³⁶⁶⁻³ apparently a contaminated material.
(EtO)(PrO)(PhO)PO. VIII. Liquid. ³⁶⁷

262 PHOSPHATES, HALOPHOSPHATES, AND THIO ANALOGS

(BuO)₂(PhO)PO. XIII. Liquid, *b*₁₈ 183–5°. ³⁷⁶

(PhO)PO(OCH₂)₂C(NO₂)CH₂OH. VI. Yellow, undistillable oil. ⁵¹⁰

(EtO)(PhO)₂PO. VIII. ³⁶⁷ X. ^{366, 368} (Neither preparation method is satisfactory, and the products are obviously impure. ³⁷⁵) Liquid, *b*₇₀ 250–63°, *b*₁₈ 211–21°, *d*₀²⁰ 1.2113. ³⁶⁶⁻⁸

(CH₂:CMe·CH₂O)(PhO)₂PO. X. Undistillable liquid, *n*_D²⁵ 1.5242. ³⁶⁹

(PhO)₃PO. X. ^{4, 47, 50} XI ^{118, 260, 387} (using ZnCl₂ catalyst), ⁴⁴⁴ (using AlCl₃ catalyst). ¹⁵⁹

XIV (with SO₃). ¹²⁶ Modified XX (from diphenyl sulfite). ¹⁴² Needles (from Et₂O-ligroin), prisms (from EtOH), *m.* 50°, ⁴⁵⁹ *m.* 49°, ^{118, 265} *b*₁₁ 245°. ¹⁵

(PhO)₂(PhS)PO. XIII. Liquid, *b*₂₅ 275–82°. ³⁷⁶

(PhS)₃PO. X. ^{52, 359} XI. ^{52, 461} XIV (using 30% H₂O₂ or HNO₃). ⁴⁶¹ Prisms, *m.* 114°, *m.* 115° (from EtOH). ^{52, 359}

(PhO)₃PSe. X. ⁵¹ XI ⁴⁴⁶ (best with a little PCl₃ added). ²⁴³ XIII. ⁵³ XXI (best with PSCl₃). ^{15, 248, 402} By heating triphenyl phosphate with potassium sulfide (many by-products). ³¹⁸ Prisms, *m.* 53°, ^{51, 402} *m.* 49–50°, ¹⁵ *m.* 49° ⁴⁴⁶ (from EtOH) *f.p.* 48°, ²⁴⁸ *b*₁₁ 245°, *b*₁ 230–40°. ²⁴⁸

(PhO)₃PSe. C (from (PhO)₂PSeCl at 180°). ⁴⁵⁵ XXI. ⁴⁵⁵ Needles, *m.* 73–4°. ⁴⁴⁶

(PhS)₃PS. X. ³⁵⁹ XI. ³⁵⁹ XXI. ³⁵⁹ Plates, *m.* 86° (from EtOH). ³⁵⁹ Undistillable.

(PhS)₃PSe. XXI. Yellow plates, *m.* 95° (from EtOH). ³⁵⁹

The following are several representative intermediates obtained in the course of synthesis of phosphate esters of polyhydroxy compounds by procedure IV:

Diphenyl 1,2-acetone-3-glycerophosphate. Oil. ¹¹⁹

Diphenyl 1,3-benzylidene-2-glycerophosphate. *M.p.* 72.5°. ¹¹⁹

Diphenyl 3',5'-benzylidene-uridine-2'-phosphate. *M.p.* 56–60°; can be hydrolyzed stepwise, losing one phenyl group in 0.5 *N* sodium hydroxide at 100°, and losing the second phenyl group in 0.25 *N* sulfuric acid. ^{116-7, 265}

***o*-C₆H₄O₂PO(OMe).** XX. Liquid, *b*₁₁ 148°. ²²

***o*-C₆H₄O₂PO(OEt).** XX. Liquid, *b*₁₂ 157°. ²²

***o*-C₆H₄O₂PS(OPh).** XXI. Liquid, *b*₁₀ 186°, which freezes and *m.* 71–2°. ²⁰

***o*-C₆H₄O₂PS(OC₆H₄Me-*o*).** XXI. Crystals, *m.* 87–8°, *b*₁₄ 197–200°. ²⁰

(2-MeC₆H₄O)₃PO. X. ⁶ XI. ^{118, 260, 421} Liquid, *b*₇₆₀ 410°, ⁴²³ *d*₄²⁵ 1.183. ¹¹⁸

(2-MeC₆H₄O)₃PS. XXI. ^{248, 455} Needles, *m.* 45°, ²⁴⁸ *m.* 45–6° (from EtOH), ⁴⁵⁵ *b*₁ 260–5°. ²⁴⁸

(2-MeC₆H₄O)₃PSe. XXI. Needles, *m.* 50–1° (from EtOH). ⁴⁵⁵

(3-MeC₆H₄O)₃PO. XI. Liquid, *b*₄₁ 258–63°, *m.* 25–6°. Bromination yields a tribromo derivative (*p*-?), *m.* 90°. ¹¹⁸

(3-MeC₆H₄O)₃PS. XXI. Needles, *m.* 40–1° (from EtOH), *b*₁₂ 270–2°. ¹²⁶

(PhO)(4-MeC₆H₄O)₂PO. X. Plates, *m.* 54° (from ligroin). ³⁴⁰

(4-MeC₆H₄O)₃PO. X. ⁴⁷ XI ^{118, 260, 421} (with magnesium catalyst). ¹⁰⁹ XX. ^{45, 497} Needles, *m.* 77°, ¹¹⁸ *m.* 77.5–78°, ²⁶⁰ *m.* 76°. ^{40, 421} Bromination yields a hexabromo derivative (2,6-?), *m.* 178°. ¹¹⁸

***o*-C₆H₄O₂PS(OC₆H₄Me-*p*).** XXI. Crystals, *m.* 71–2°, *b*₁₂ 206–8°. ²⁰

(PhO)₂(4-MeC₆H₄O)PS. X. Prisms, *m.* 69° (from EtOH). ⁵³

(PhO)(4-MeC₆H₄O)₂PS. X. Prisms, *m.* 54° (from EtOH). ⁵³

(4-MeC₆H₄O)₃PS. X. ⁵³ XXI. ⁴⁵⁵ Needles, *m.* 93–4° (from EtOH), ⁴⁵⁵ *m.* 87°. ⁵³

(4-MeC₆H₄O)₃PSe. XXI. Needles, *m.* 111–2° (from EtOH). ⁴⁵⁵

(4-MeC₆H₄S)₃PS. X. ⁵³ XI. ⁴⁵⁵ XVI. ⁴⁵⁵ XXII. ⁴⁵⁵ Plates, *m.* 121–2° (from EtOH), ⁵³ *m.* 119–20°. ⁴⁵⁵

(2,4-Me₂C₆H₃O)₃PO. XI. Viscous oil. ⁵¹⁸

- (3,4-Me₂C₆H₃O)₃PO. XI. Viscous oil.³¹⁸
- (2,5-Me₂C₆H₃O)₃PO. XI. Crystals, m. 77°.¹¹⁸
- (2-CH₂:CH·CH₂C₆H₄O)(PhO)₂PO. XIII. Liquid, b_{6.5} 250–60°, n_D²⁵ 1.5640.¹²⁴
- (2-CH₂:CH·CH₂C₆H₄O)₂(PhO)PO. XIII. Liquid, b₆ 254–62°, n_D²⁵ 1.5669.¹²⁴
- (2-CH₂:CMe·CH₂C₆H₄)₂(PhO)PO. XIII. Liquid, b_{7.5} 267–9°, n_D²⁵ 1.5647.¹²⁴
- (4-*tert*-BuC₆H₄O)(PhO)₂PS. XXI. Liquid, b₇ 252–67°.³⁷³
- (4-*tert*-BuC₆H₄O)₃PO. XI. Crystals, m. 101° (from EtOH), b₄ 315–7°.⁹⁹
- (4-*tert*-BuC₆H₄O)(PhO)₂PO. XIII. Liquid, b₆ 261°.⁹⁹
- (4-*tert*-BuC₆H₄O)₂(PhO)PO. XIII. Liquid, b_{6.5} 281°.⁹⁹
- (4-*tert*-BuC₆H₄O)(2-MeC₆H₄O)₂PO. XIII. Liquid, b₂₀ 284°.⁹⁹
- (4-*tert*-BuC₆H₄O)₂(2-CH₂:CH·CH₂C₆H₄O)PO. XIII. Liquid, b₈ 291–7°.¹²⁴
- (2-Me-5-*iso*-PrC₆H₃O)(PhO)₂PS. XXI. Liquid, b_{7.5} 240–8°.³⁷³
- (2-Me-5-*iso*-PrC₆H₃O)₃PO. XI. XX. Prisms or plates, m. 75°.³¹⁸ m. 71.5–2°.²⁸⁹
- (2-*iso*-Pr-5-MeC₆H₃O)₃PO. XI. Prisms, m. 59° (from EtOH).^{203, 318}
- (4-*tert*-AmC₆H₄O)₃PO. XI. Viscous oil.³¹⁸
- (2-Me-4-*tert*-BuC₆H₃O)₂(PhO)PO. XIII. Liquid, b₈ 280–5°, n_D⁶⁰ 1.5272.³⁷⁰
- (2-Me-4-*tert*-BuC₆H₃O)(4-*tert*-BuC₆H₄O)₂PO. XIII. Liquid, b₈ 314–8°.³⁷⁰
- (2-Me-4-*tert*-BuC₆H₃O)₂(4-*tert*-BuC₆H₄O)PO. XIII. Liquid, b₈ 310–4°.³⁷⁰
- (2-Me-4-*tert*-BuC₆H₃O)₃PO. XI. Liquid, b₈ 304–8°, n_D⁶⁰ 1.5182.³⁷⁰
- (2-*iso*-Pr-4-*tert*-Am-5-MeC₆H₂O)₃PO. VIII (from triphenyl phosphate). Oil.³¹²
- (2,6-(CH₂:CHCH₂)₂C₆H₃O)(PhO)₂PO. XIII. Liquid, b₅ 254–8°, n_D²⁵ 1.5637.¹²⁴
- (Me₃C·CH₂·CMe₂C₆H₄O)₃PO. (Para isomer, presumably). XI. Oil, b₁₂ 361–5°.¹⁰¹
- (1-C₁₀H₇O)(EtO)₂PO. XIII. Undistillable liquid, d₀¹⁸ 1.0441.³²¹
- (1-C₁₀H₇O)₂(EtO)PO. XIII. Plates, m. 31–2°.³²¹
- (1-C₁₀H₇O)₃PO. X.^{47, 118} XI.^{6, 260, 321} XX.^{26, 166, 443} Crystals (from benzene, EtOH, or Me₂CO), m. 149–50°.⁴³⁰ m. 148–9°.⁸ m. 145°.^{118, 221, 443} m. 144.5–45°.³⁶⁰
- (2-C₁₀H₇O)(EtO)₂PO. XIII. Liquid, d₀¹⁸ 1.0439.³²¹
- (2-C₁₀H₇O)₂(PhO)PO. XI (with AlCl₃ catalyst). Oil, b₉ 300° (decomposition).¹⁵⁹
- (2-C₁₀H₇O)₃PO. X.⁴⁷ XI.^{159, 260} X.¹¹⁸ XX.^{26, 47, 443} Needles, m. 111°.^{47, 118} m. 110–1°.^{26, 159, 260} m. 108°.⁴⁴³
- (2-PhC₆H₄O)(PhO)₂PO. XIII. Oil, b₁₁ 289–90°.⁹⁷
- (2-PhC₆H₄O)(PhO)₂PS. XXI. Oil, b₆ 275–81°.³⁷³
- (2-PhC₆H₄O)(PhO)(2-MeC₆H₄O)PO. XIII. Oil, b₁₁ 286–8°.⁹⁷
- (2-PhC₆H₄O)(2-MeC₆H₄O)₂PO. XIII. Oil, b₂₃ 315°.⁹⁷
- (2-PhC₆H₄O)(2-CH₂:CH·CH₂C₆H₄O)₂PO. XIII. Oil, b₆ 293–6°, n_D²⁵ 1.5872.¹²⁴
- (2-PhC₆H₄O)(4-*tert*-BuC₆H₄O)₂PS. XI. Oil, b_{7.5} 316–30°.³⁷³
- (2-PhC₆H₄O)(2-C₁₀H₇O)₂PO. XIII. Undistillable liquid.⁹⁷
- (2-PhC₆H₄O)₂(PhO)PO. XIII. Liquid, b_{6.5} 273–5°.⁹⁷
- (2-PhC₆H₄O)₂(PhO)PS. XI. Liquid, b₁₀ 320–30°.³⁷³
- (2-PhC₆H₄O)₃PO. XI (using MgCl₂ catalyst). Crystals, m. 114°.⁹⁵
- (2-PhC₆H₄O)(4-*tert*-BuC₆H₄O)(2-Ph-4-*tert*-BuC₆H₃O)PO. XIII. Oil, b₆ 323–45°.³⁷³
- (2-PhC₆H₄O)₂(2-Me-4-*tert*-BuC₆H₃O)PO. XIII. Liquid, b₈ 340–5°.³⁷⁰
- (2-PhC₆H₄O)(2-Ph-4-*tert*-BuC₆H₃O)₂PO. XIII. Liquid, b_{7.5} 356–60°.³⁷³
- (2-Ph-4-*tert*-BuC₆H₃O)(4-*tert*-BuC₆H₄O)₂PO. XIII. Liquid, b₆ 300–25°.³⁷³
- (2-Ph-4-*tert*-BuC₆H₃O)₃PO. XI. Liquid, b_{7.5} 344–6°.³⁷³
- (2,4-Ph₂·C₁₀H₅O)₃PO. XX. Crystals, m. 130° (from benzene), m. 198–9° (from CCl₄-EtOH).²⁴⁶
- (3-PhC₆H₄O)(PhO)₂PO. XIII. Liquid, b₈ 293°.¹³⁰
- (3-PhC₆H₄O)(2-MeC₆H₄O)₂PO. XIII. Liquid, b₅ 284–98°.¹³⁰
- (3-PhC₆H₄O)₂(PhO)PO. XIII. Liquid, b₈ 345°.¹³⁰

264 PHOSPHATES, HALOPHOSPHATES, AND THIO ANALOGS

- (3-PhC₆H₄O)₃PO. XI. Crystals, m. 84–6°, b₁₀ 384°. ¹²⁰
 (4-PhC₆H₄O)(PhO)₂PO. XIII. Liquid, b₁₀ 302–9°. ¹²¹
 (4-PhC₆H₄O)(2-MeC₆H₄O)₂PO. XIII. Liquid, b₆₋₇ 303–5°. ¹²¹
 (4-PhC₆H₄O)₂(PhO)PO. XIII. Liquid, b₆₋₇ 360–1°, freezing on cooling; m. 88–90°. ¹²¹
 (4-PhC₆H₄O)₂(2-MeC₆H₄O)PO. XIII. Liquid, b₆ 353°. ¹²¹
 (4-PhC₆H₄O)₂(2-Me-4-*tert*-BuC₆H₃O)PO. XIII. Liquid, b₈ 378–85°. ³⁷⁰
 (4-PhC₆H₄O)₃PO. XI. Crystals, m. 137.5°. ¹²¹
 (2-C₆H₁₁·C₆H₄O)(PhO)(4-*tert*-BuC₆H₄O)PO. XIII. Liquid, b₆ 293–300°. ⁹⁹
 (4-C₆H₁₁·C₆H₄O)₂(4-*tert*-BuC₆H₄O)PO. XIII. Crystals, m. 81.5°. ⁹⁹
 (2-C₆H₁₁-4-PhC₆H₃O)₂(PhO)PO. XIII. Liquid, b_{9,5} 371–95°. ³⁷²
 (2-Ph-4-C₆H₁₁·C₆H₃O)₂(PhO)PO. XIII. Liquid, b_{7,5} 340–4°. ³⁷²
 (2-C₆H₁₁-4-*tert*-BuC₆H₃O)₂(4-PhCMe₂C₆H₄O)PO. XIII. Liquid, b₁₀ 378–90°. ³⁷²
 (4-PhCH₂C₆H₄O)₃PO. XX. Needles, m. 93–4° (from CHCl₃). ³⁹⁴
 (C₆H₁₁O)(iso-AmO)₂PO. XIII. Liquid, b_{0,5} 142°. ²⁷⁶
 Trimenthyl phosphate. X (best). ^{362, 363} XI. ³⁶³ XX. ³⁶³ VI. ³⁶³ Plates, m. 86°; ^{362, 363} levo derivative: [α]_D –100° (in MePh). ³⁶³
 Trifenchyl phosphate. Levo derivative. X. Crystals, m. 160°. ²⁷⁰
 Tri-trans-2-decahydronaphthyl phosphate. X. Crystals, m. 159°. ²⁷⁰
 Tri-3-phenanthryl phosphate. X. Plates, m. 180–2° (from MePh). ⁴⁸⁶

2. HALOGEN DERIVATIVES

- (EtO)₂(2-ClC₆H₄O)PO. Liquid, b₂ 140°. ¹⁰⁹
 (PhO)₂(2-ClC₆H₄O)PO. XIII. Liquid, b₄ 236°. ⁹⁶
 (PhO)(2-ClC₆H₄O)₂PO. XIII. Liquid, b₄ 254°. ¹⁰⁰
 (2-ClC₆H₄O)₃PO. XI. Crystals, m. 37°, b_{17,5} 309°. ⁹⁶
 (2-MeC₆H₄O)₂(2-ClC₆H₄O)PO. XIII. Liquid, b₇ 272–3°. ¹⁰⁰
 (2-MeC₆H₄O)(2-ClC₆H₄O)₂PO. XIII. Liquid, b₁₅ 268–70°, ¹⁰⁰ b₁₅ 312–15° ⁹⁶(?).
 (3-MeC₆H₄O)₂(2-ClC₆H₄O)PO. XIII. Liquid, b₁₁₋₂ 279–80°. ¹⁰⁰
 (4-MeC₆H₄O)₂(2-ClC₆H₄O)PO. XIII. Crystals, m. 52–3°, b₉₋₁₀ 282–4°. ¹⁰⁰
 (2-C₁₀H₇O)(2-ClC₆H₄O)₂PO. XIII. Liquid, b₇₋₁₀ 315–30°. ⁹⁶
 (4-C₆H₁₁·C₆H₄O)(2-ClC₆H₄O)₂PO. XIII. Liquid, b₅ 315–25°. ⁹⁶
 (2-Me-5-iso-PrC₆H₃O)(3-ClC₆H₄O)₂PS. XIII. Liquid, b_{7,5} 274–82°. ³⁷³
 (EtO)₂(4-ClC₆H₄O)PO. Liquid, b₂ 142°. ¹⁰⁹
 (2-ClC₆H₄O)(4-ClC₆H₄O)₂PO. XIII. Liquid, b_{11,5} 290°. ⁹⁶
 (4-ClC₆H₄O)₃PO. X. ^{47, 55} XI. ^{118, 376, 509} By heating triphenyl phosphate with sulfonyl chloride in the presence of iron. ¹⁹⁷ Needles, m. 117°, ¹¹⁸ m. 113°, ¹⁹⁷ m. 112–3°, ³⁷⁶ m. 112°, ⁸ m. 99–100° (crude), ^{47, 55} b₁₈ 292–5°. ³⁷⁵
 (4-ClC₆H₄O)₃PS. XXI (from the corresponding phosphite or selenophosphate). ⁴⁵⁵
 The earlier preparation X ⁵¹ is said to be in error. ⁴⁵⁵ Needles, m. 85–6° (from EtOH); ⁴⁵⁵ plates, m. 113–4°(?). ⁵¹
 (4-ClC₆H₄O)₃PSe. XXI. Needles, m. 88° (from EtOH). ^{358, 455}
 (4-ClC₆H₄O)₂(4-*tert*-BuC₆H₄O)PO. XIII. Liquid, b₄ 287°. ⁹⁹
 2-(1-ClC₁₀H₆O)₃PO. X. ⁴⁷ XX. ¹⁷¹ Needles, m. 152° (from EtOH). ^{47, 171}
 (4-BrC₆H₄O)₃PO. Modified XX (from phenyl acetate and PBr₅; poor yield). ⁵⁴
 By bromination of triphenyl phosphate at 180°. ³⁴⁷ Scales, m. 109°, ¹¹⁸ m. 101°. ^{54, 347}
 (2-iso-Pr-4-Br-5-MeC₆H₂O)₃PO. XX. Needles, m. 94–5° (from EtOH-Et₂O). ⁴⁰⁴
 (2-Me-4,6-Cl₂C₆H₃O)₃PO. XX. Needles, dec. 248°. ¹³⁷
 (2,4-Br₂C₆H₃O)(PhO)₂PO. XIII. Liquid, b₈ 273–83°, ²⁵ n_D²⁵ 1.5992. ¹³³
 (2,4-Br₂C₆H₃O)(PhO)(2-MeC₆H₄O)PO. XIII. Liquid, b₈ 270–85°, ²⁵ n_D²⁵ 1.5934. ¹³³
 (2,4-Br₂C₆H₃O)(2-MeC₆H₄O)₂PO. XIII. Liquid, b₆ 290–300°, ²⁵ n_D²⁵ 1.5939. ¹³³

- (2,4-Br₂C₆H₃O)(2-Me-5-iso-PrC₆H₃O)₂PO. XIII. Liquid, b₈ 295–305°. ¹²³
 (2,4,6-Cl₃C₆H₂O)₂(MeO)PO. V. Crystals, m. 132–3° (from dil. EtOH). ^{501, 502}
 (2,4,6-Cl₃-3-MeC₆HO)₃PO. XX. Needles, m. 230° (from AcOH). ¹²⁸
 Br₄C₆O₂PO(OPh). XIII. Resinous solid, m. about 110°. ⁵⁰⁷
 2-(1,6-Br₂C₁₀H₅O)₃PO. XX. Crystals, dec. 200–1°. ²⁶
 (2-Cl₂CH·C₆H₄O)₃PO. XX (from salicylaldehyde). ⁴⁶⁸ By chlorination of tri-2-tolyl phosphate at 160–80°. ^{422, 423} Needles, m. 78°. ⁴⁶⁸
 (2-Cl₃C·C₁₀H₅O)(EtO)₂PO. XIII. Crystals, m. 63° (from ligroin). ⁴⁹⁴
 (2-CH₂:CCl·CH₂·C₆H₄O)(2-MeC₆H₄O)₂PO. XIII. Liquid, b₇ 258–67°. ¹²⁴

3. HYDROXY COMPOUNDS AND THEIR DERIVATIVES

- (3-HOC₆H₄O)₃PO. XX (from resorcinol). Monohydrate, crystals, m. 75°. ⁴⁴⁷
 (4-HOC₆H₄O)₃PO. XX (from hydroquinone). Needles, m. 149° (from water). ⁴⁴⁷
 (2-MeOC₆H₄O)₃PO. XI. ¹¹⁸ XX. ¹⁸⁸ Prisms, m. 91° (from EtOH). ^{118, 188}
 (2-MeOC₆H₄O)₂(4-PhC₆H₄O)PO. XIII. Liquid, b₁₂ 327°. ¹²¹
 (2-MeOC₆H₄O)(o-C₆H₄O)₂PS. XXI. Crystals, m. 93–4°. ²⁹
 (2-EtOC₆H₄O)₃PO. XI. Crystals, m. 131–2°. ³⁵⁴
 (2-MeO-4-CH₂:CH·CH₂C₆H₃O)₃PO. X. Yellow undistillable oil. ²⁰⁰

4. ALDEHYDE AND ACID DERIVATIVES

- (OHC(4-?)·C₆H₄O)(EtO)₂PO. Liquid, b_{0,8} 160°. ¹⁰⁹
 (OHC(2-?)·C₆H₄O)(EtO)₂PO. Liquid, b₁ 146°. ¹⁰⁹
 (2-EtO₂C·C₆H₄O)(EtO)₂PO. Liquid, b₁ 156°, b₂ 180°. ¹⁰⁹
 (4-EtO₂C·C₆H₄O)(EtO)₂PO. Liquid, b₂ 175°. ¹⁰⁹
 (2-MeO₂C·C₆H₄O)(PhO)₂PO. XIII. Liquid, b_{7,6} 254–65°. ³⁷¹
 (2-MeO₂C·C₆H₄O)(2-PhC₆H₄O)₂PO. XIII. Liquid, b₈ 340–51°. ³⁷¹
 (2-iso-BuO₂C·C₆H₄O)(2-PhC₆H₄O)₂PO. XIII. Crystals, m. 99–102°, b₇ 333–6°. ³⁷¹
 (2-MeO₂C·C₆H₄O)₂(PhO)PO. XIII. Liquid, b₅ 274–8°. ³⁷¹
 (2-MeO₂C·C₆H₄O)₂(2-ClC₆H₄O)PO. Liquid, b_{7,6} 304–15°; XIII. ³⁷¹
 (2-MeO₂C·C₆H₄O)₂(4-tert-BuC₆H₄O)PO. Liquid, b_{7,8} 304–15°; XIII. ³⁷¹
 (2-MeO₂C·C₆H₄O)₃PO. XI. Liquid, b_{7,6} 294–309°. ³⁷¹
 (2-(1-HO₂C·C₁₀H₆O))(EtO)₂PO. XIII. Crystals, m. 113° (from EtOH). ⁴¹⁷

5. STEROL DERIVATIVES

- Dimethyl 17-testosterone phosphate.** XXIV. By oxidation of the corresponding androsterone-3,17-diol phosphate with chromic acid. Crystals, m. 152–3°. Oxime, dec. 185°. ³⁷⁶
Diethyl 17-testosterone phosphate. XXIV. Oil, b. 160° (in high vacuum). ³⁷⁶
Dimethyl 17-((5,6)androsterone-3,17-diol) phosphate. XXIV. Crystals, m. 192–3° (from dil. MeOH). ³⁷⁶
Diethyl 17-((5,6)androsterone-3,17-diol) phosphate. XXIV. Crystals, m. 165° (from benzene). ³⁷⁶
Dipropyl 17-((5,6)androsterone-3,17-diol) phosphate. XXIV. Crystals, m. 101° (from benzene-ligroin). ³⁷⁶
Dibutyl 17-((5,6)androsterone-3,17-diol) phosphate. XXIV. Very unstable substance. ³⁷⁶
Diergosteryl 2-chloroethyl phosphate. XIII. Crystals, m. 165–7°. ²¹²
Dicholesteryl 2-chloroethyl phosphate. XIII. Crystals, m. 158°. ²¹²

The following compounds are reported as (S,S)-dicholesteryl derivatives, prepared from the disodium salt of alleged (S,S)-dicholesteryl-orthodithiophosphate: (RS)₂-

266 PHOSPHATES, HALOPHOSPHATES, AND THIO ANALOGS

(NaO)₂POH(?), by reaction with the corresponding halogen compounds (bromides).⁴⁸¹

(O)-Cinnamyl (S,S)-dicholesteryl dithiophosphate. Crystals, m. 152–3°.

(O)-Benzyl (S,S)-dicholesteryl dithiophosphate. Crystals, m. 168–70°.

The (S,S) structure of these esters may be questioned on the basis of the uncertain structure of the above mentioned sodium salt.

6. NITROGEN DERIVATIVES

(2-O₂N·C₆H₄O)(EtO)₂PO. Liquid, b₂ 176°.¹⁰⁹

(2-O₂N·C₆H₄O)₃PO. XX. Needles, m. 126° (from xylene).²⁰⁴

(3-O₂N·C₆H₄O)(EtO)₂PO. Liquid, b₁ 172°.¹⁰⁹

(4-O₂N·C₆H₄O)(EtO)₂PO. X. XIII. By nitration of the corresponding phenyl derivative at 0° with fuming nitric acid.^{109, 250} Liquid, b₁ 173°.¹⁰⁹

(4-O₂N·C₆H₄O)(EtO)₂PS. X. Liquid,^{110, 216, 225} b₂ 180°,¹¹⁰ b_{0, 6} 157–62°, n_D^{25} 1.5370.²²⁵

(4-O₂N·C₆H₄O)₂(EtO)PO. By prolonged boiling of the triester with ethanol. Needles, m. 135° (from EtOH).⁴²¹ This substance has been questioned; its true structure is believed to be that of di-*p*-nitrophenyl phosphate.²⁶⁵

(4-O₂N·C₆H₄O)₃PO. X.⁴²¹ XX.²⁰⁴ Best: by nitration of triphenyl phosphate with fuming nitric acid below 0°.^{265, 421} Some 2-nitro isomer is also formed (not isolated).²⁶⁵ Crystals, m. 155° (from AcOH).²⁶⁵ m. 155°,⁴²¹ m. 148°.²⁰⁴

(3-Me-4-O₂N·C₆H₃O)(EtO)₂PO. Liquid, b₂ 149°.¹⁰⁹

(2-EtO₂C-4-O₂N·C₆H₃O)(EtO)PO. Liquid, b₄ 190°.¹⁰⁹

(2,4-(O₂N)₂C₆H₃O)₃PO. By nitration of triphenyl phosphate with mixed acid at 80°. Crystals.²³²

(4-PhN:NC₆H₄O)₃PO. XX. Yellow needles, m. 148° (from Me₂CO).²⁰²

(4-(2-MeC₆H₄N:N)C₆H₄O)₃PO. XX. Orange-red needles, m. 116°.³⁰¹

(4-(4-MeC₆H₄N:N)C₆H₄O)₃PO. XX. Needles, m. 140° (from Me₂CO).³⁰¹

Triquinine phosphate. XI. Crystals, dec. 260° (from CHCl₃).⁵¹¹

7. DIPHOSPHATES

m-C₆H₄(OPO(OEt)₂)₂. XIII. Undistillable oil.³¹¹

p-C₆H₄(OPO(OEt)₂)₂. XIII. Undistillable oil.³¹¹

o-C₆H₄(OPO(O₂C₆H₄))₂. XI (from pyrocatechol).^{24, 311} Plates, m. 230°, b₁₂ 300°.^{24, 311}

o-C₆H₄(OPS(O₂C₆H₄))₂. XXI. Needles, m. 114–5° (from ligroin).³⁵

4-Me₃C·C₆H₃-(1,2)-(OPO(O₂(1,2)C₆H₃-4-CMe₃))₂. XI. Solid, b₁₀ 335–7°,¹⁸⁶ b₁₀ 333–7°.¹²²

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270 PHOSPHATES, HALOPHOSPHATES, AND THIO ANALOGS

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274 PHOSPHATES, HALOPHOSPHATES, AND THIO ANALOGS

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276 PHOSPHATES, HALOPHOSPHATES, AND THIO ANALOGS

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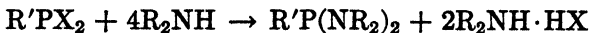
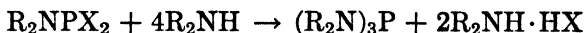
Compounds with Phosphorus to Nitrogen Bonds

Compounds in this chapter are the various substances that contain the phosphorus to nitrogen linkage, single, double, or semipolar. These substances are represented by the amides of phosphorous acid, phosphoric acid, their halides and esters, phosphonic acids, and the thio analogs of the foregoing classes. In addition, a variety of imido derivatives of these classes are included, as are the substances belonging to the category of phosphinimines, which are essentially semipolarly linked substances.

METHODS OF PREPARATION

I. Reaction of halides of trivalent phosphorus with primary and secondary amines

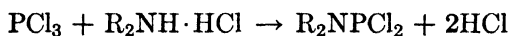
Phosphorus trihalides, primary and secondary halophosphites, as well as halophosphines, react with primary and secondary amines to form haloamidophosphites or amidophosphites (or amides of phosphonous acids in the case of halophosphines). The basic equations, which are given below, indicate the customary use of two moles of the amine for each replaceable halogen atom. However, a number of factors modify the final products in many instances, and a number of the primary products, expected from such reactions, cannot be isolated.^{75, 77, 78, 83}



The reactions are performed in inert solvents (ether or ligroin) at low or moderate temperatures, and the products are isolated after filtration of the amine salt. Although the reactions with secondary amines

proceed essentially as shown above, the similar reactions with primary amines deviate very seriously from the expected course. The initial reactions probably yield the expected products, but these materials, characterized by a link, NH-PX , are very readily transformed into other substances by warming or by the presence of bases (amine excess). Usually the transformation products are imidophosphites (see Section VIII). Such transformations occur so readily with the primary aromatic amines that the initial reaction products cannot be isolated.^{41, 77, 78, 89} In the aliphatic series, the lower members of the haloamidophosphites can be isolated (in poor yields), but none of the higher members, because of the above-mentioned secondary reaction that occurs on attempted distillation.

The foregoing reaction scheme applied to phosphorus halides that have more than one halogen atom usually leads to a mixture of the possible products, unless complete substitution is desired and an excess of the amine is used. It is possible to control such reactions rather satisfactorily, with restriction to monosubstitution, in the case of secondary amines. Instead of the free amine, its hydrochloride is used and the mixture is refluxed for several hours.⁷⁷ (Michaelis.)



II. Reaction of primary or secondary amines with compounds containing the phosphoryl halide group

Primary and secondary amines react smoothly with phosphorus oxyhalides (usually phosphorus oxychloride is used), halophosphates, haloamidophosphates, and phosphonyl halides and form the corresponding amides. The reactions proceed similarly to the reaction schemes given in the previous section, except for the change of the reagents from P-X to P(O)X derivatives. The reactions are carried out in inert solvents under conditions similar to those used for the trivalent analogs. Somewhat more elevated temperatures are usually necessary to complete the substitution to phosphoric triamides, starting with phosphorus oxychloride or the amido derivatives, because of their lower reactivity. Some of the typical reactions are shown below.^{9, 26, 77} (Michaelis.)



Again a mixture of products may be expected at the intermediate stages of phosphorylation.⁷⁷ However, satisfactory preparations of N-arylamidodichlorophosphates, $\text{RNHP}(\text{O})\text{Cl}_2$, have been obtained by slow addition of the amine (2 moles) to phosphorus oxychloride in cold benzene.²⁶ Secondary amines react as expected even on heating, but the primary amidohalophosphates, $\text{RNHP}(\text{O})\text{Cl}_2$ and $(\text{RNH})_2\text{P}(\text{O})\text{Cl}$, derived from primary amines should not be heated unduly during preparation or isolation, if the imide formation is to be avoided (see Section VI).

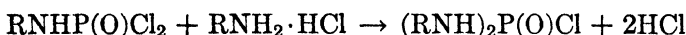
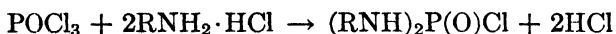
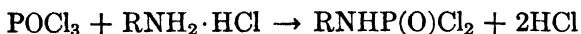
The amidohalophosphates, as may be expected, can be used for the formation of the diamido and triamido derivatives, with similar or different radicals,^{26,77} in similar reactions. The excess of the amine necessary for such reactions may be replaced by tertiary base. Pyridine has been used as a rule, but then it was found that the same excess of the amine was needed for satisfactory yields.^{8,10} Possibly other tertiary bases like 2,6-lutidine may be more efficient (see Chapter 9). (Audrieth, Toy.) Use of phosphoryl dichlorofluoride permits rather clean diamidation, and the resulting diamidofluorophosphates are obtained in good yields.⁴⁴ The lower activity of the fluorine permits such a differential action.⁶⁸

Although the various amines or ammonia give the best yields of completely amidated products most satisfactorily in dry inert solvents, aqueous solutions may be used in the reactions of chlorophosphates or aryl dichlorophosphates (which are fairly stable to hydrolysis). Amines give satisfactory yields under these conditions, but ammonium hydroxide as a rule does not provide yields of much over 50% of theoretical; an appreciable amount of the halides is converted to the free acids (see Section XXIII). In such cases, either liquid ammonia or dry ammonia gas is preferable.^{8,9,59} The customary use of carbon tetrachloride or chloroform is not very satisfactory because of side reactions that take place when the reaction mixture must be warmed to complete triamidation reactions with phosphorus oxychloride. Hydrocarbon solvents are preferable both for this reason and for the much easier removal of residual amounts of amine hydrochlorides, which are appreciably soluble in chlorinated solvents. Low-boiling petroleum fractions are best in such cases. The final removal of traces of the salts, which may be still retained, is essential if distillable products are to be obtained. The older preparations of the phosphoric amides could not be distilled for this reason.^{77,78} Such removal is readily performed by stirring the triamidophosphate in inert solvent with warm alkali, used in small volume and high concentration; this is useful for the lower alkyl members that have high solubility in aqueous solvents.⁵⁹

As may be expected, deficient amounts of diamines or hydrazine react with aryl dichlorophosphates to form the corresponding cyclic diamidophosphates or cyclic dihydrazidodiphosphates.¹² (Autenrieth.)

III. Reaction of amine hydrochlorides with compounds containing the phosphoryl halide group

The reactions discussed in this section are mostly commonly applied to the preparations of primary amidodichlorophosphates or secondary diamidochlorophosphates, from phosphorus oxychloride or, in the second instance, from primary amidodichlorophosphates.⁷⁷



These reactions are carried out under conditions of mild reflux, continued for several hours until the amine salt suspension becomes a clear solution.^{77, 78, 142} The slowness of the attack permits a cleaner preparation of the individual halogen derivatives than is generally possible by the methods of Section II. However, undue heating must be avoided, especially for the synthesis of the monohalo derivatives. Unless the heating is terminated at the attainment of a clear solution the decomposition reactions, which result in the imido derivatives, occur. The final product is quite readily controlled by the ratio of the ingredients, and the first equation conditions are best achieved with an excess of phosphorus oxychloride. A small amount of a high-boiling solvent, such as xylene, is customarily added to the reaction mixture to preserve mobility and prevent local overheating. An economical combination of methods II and III may be used, in which the free amine and the phosphorus halide are permitted to react at low temperature and the mixture, which now contains the amine salt, is heated as described above. In this manner the complete utilization of the amine is achieved.⁷⁷ The rather drastic conditions preclude the use of this method with alkyl halophosphates, but a few aryl ester derivatives have been converted to ester amidophosphates.^{77, 101} (Michaelis.)

IV. The reaction of primary and secondary amines with compounds containing the thionophosphoryl halide group

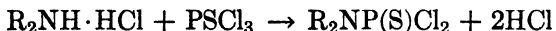
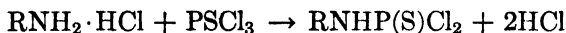
The reactions described in Section II can be duplicated with the aliphatic amines and thionophosphoryl halide derivatives, thiophosphoryl chloride (PSCl_3), N-alkyl (or dialkyl)-amidodihalothionophosphates (RNHP(S)X_2 or $\text{R}_2\text{NP(S)X}_2$), as well as with the primary or

secondary halophosphates of the thiono series (example, ROP(S)X_2). Usually, the reactions require somewhat more drastic conditions than are needed for the oxygen analogs. Primary aromatic amines usually do not yield clean-cut products because of side reactions that yield the imido derivatives; the secondary alkylaryl amines usually react normally. The triamidothiono derivatives are quite readily made when a substantial excess of the amine is used (somewhat over 6 moles) with thiophosphoryl chloride, the reaction being completed by moderate heating.^{10, 77, 78}

The imido derivative formation, mentioned above, prevents the preparation of mixed aromatic derivatives of the triamides.^{24, 77}

V. The reaction of amine hydrochlorides with thiophosphoryl halides

Rather few applications of this reaction have been successful. The conditions, which are identical with those given in Section III for the oxygen analogs, favor the formation of the imido derivatives as a rule. Thus heating primary aromatic amine hydrochlorides with thiophosphoryl chloride yields N-aryl-imidochlorothionophosphates, RN:PSCl . However, a number of the aliphatic derivatives were made in yields superior to those attained by the direct amine action (see Section IV).^{77, 78} (Michaelis.)



VI. Thermal decomposition reactions

The several reactions included in this section are actually secondary reactions that may be encountered in the preparation of the amido derivatives by the methods of the previous sections. However, they may be used deliberately for the synthesis of the imido derivatives. As a rule the reactions proceed at similar temperatures, which are in the range of 170 to 200° or somewhat higher.^{77, 78} (Michaelis.)

VIA. Thermal decomposition of phosphoric amides (primary amine derivatives). The decomposition takes the form of cleavage of the primary amine with the resulting formation of phosphoric imido-amides.^{77, 78, 92, 100} The reaction is conducted at somewhat above 200° and should be run under reduced pressure to eliminate the resulting amine rapidly. As a rule, the aliphatic products are monomeric, but the substances from the aromatic amines are obtained in associated form. The poor solubility usually precludes molecular weight determinations, but the few that were measured gave substantially dimeric values.^{25, 78}



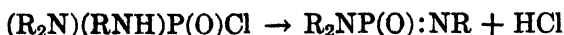
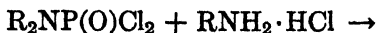
VIB. Thermal decomposition of thionophosphoric amides (primary amine derivatives). In a reaction that is a direct analog to those given in the previous subsection, the thionophosphoric amides of primary amines are readily converted to the thionophosphoric imido-amides. The association tendency is higher in these derivatives than in the oxygen analogs, and even the aliphatic members show dimeric molecular weights in freezing point determinations, although monomeric values are obtained by the boiling point methods. The products usually have better organic solubility than the oxygen analogs.⁷⁸ (Michaelis.)



VIC. Thermal decomposition of diamidochlorophosphates (primary amine derivatives). Diamidochlorophosphates decompose on prolonged strong heating, generally in the vicinity of 200°, and yield phosphoric imidoamide. The reaction affects only substances based on the primary amines in ways similar to those indicated in the previous subsections. In effect, the product is formed by a loss of hydrogen chloride across the phosphorus to nitrogen linkage. The products are identical in comparison with the corresponding substances obtained from phosphoric amides.⁷⁸ (Michaelis.)



VID. Thermal decomposition of crude amidochlorophosphates. The reaction described in the previous section is usually run in a simplified manner, in which the starting material is not isolated in the pure individual state. It is usually more convenient to begin either with phosphorus oxychloride and two molar equivalents of the primary amine hydrochloride or with an amidodichlorophosphate and one equivalent of the amine salt. Such mixtures are heated in the vicinity of 150 to 170° to complete the initial reaction (see Section III), and the crude oil is subjected to further and more drastic heating until the decomposition of the diamidochlorophosphate is complete.⁷⁸ It is possible to prepare mixed derivatives if the original amidodichlorophosphate is a derivative of a secondary amine and cannot enter the cleavage reaction per se.^{78, 92} (Michaelis.)



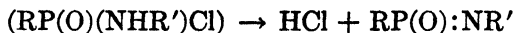
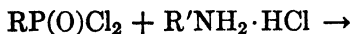
The thermal decomposition of crude amidodichlorophosphates of primary amines proceeds in an analogous manner, when the mixtures

of phosphorus oxychloride and primary amine hydrochloride are heated as prescribed for the synthesis of the amidodichlorophosphates (see Section III) and the reaction is continued for many hours at progressively higher temperatures (usually the final stage requires 230 to 240°).⁷⁸ The loss of hydrogen chloride that takes place results in the formation of imidochlorophosphates, such as N-phenylimidochlorophosphate, PhN:P(O)Cl , from aniline.

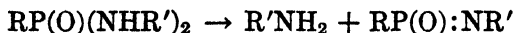


The products are usually associated; the few actual determinations that have been made indicate dimerization. As a rule significant amounts of the corresponding phosphoric imidoamide are formed simultaneously; these are separated by taking advantage of better solubility of the halides in organic solvents. Although these by-products may arise from some diamidochlorophosphates formed in the initial reaction, the indications are that some disproportionation takes place and that this may be the real source of the amidoimido derivatives. The theory of disproportionation is supported by the formation of similar mixtures, with predominant content of the phosphoric imidoamides, upon similar high-temperature treatment of the amidodichlorophosphates, RNHP(O)Cl_2 .^{78, 92}

VIE. Thermal décomposition of amidophosphonyl chlorides. These reactions bear a considerable analogy to those given in the previous section. Although small-size preparations of imidophosphonates are accomplished by thermal decomposition of phosphonamides RP(O)(NHR')_2 in a manner similar to the methods of Section VIA, the larger runs are best performed in a manner similar to the method of Section VID. The phosphonyl dichloride is heated gradually for 2 or 3 days with one equivalent of primary amine hydrochloride, with the concluding stages being conducted at about 200°. A small amount of xylene is advisable to prevent local overheating.⁷⁸ (Michaelis.)

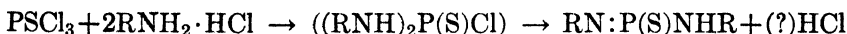


VIF. Thermal decomposition of phosphonodiamides. Diamides of primary phosphonic acids formed from the primary amines decompose on prolonged strong heating to above 200° and yield the imido derivatives in a manner similar to the reactions in Section VIA.



VIG. Thermal decomposition of amidothionochlorophosphates. A reaction analogous to those described in Section VID may

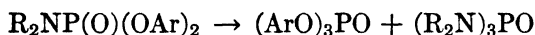
be conducted with thiophosphoryl chloride and primary aromatic amine hydrochlorides. When equimolar mixture of the reagents is heated to gentle reflux for several days, the slow formation of the product results in the formation of the amidoimido derivatives if the action is interrupted after 2 or 3 days. If the action is continued to completion of the evolution of hydrogen chloride, the imidothionochlorides form. The slow rate of the reaction permits such selectivity, which is not usual among the oxygen analogs. It is probable that the reaction proceeds via the normally expected halo intermediates. Usually, the reaction is run with an excess of thiophosphoryl chloride, which preserves fluidity of the mixture and serves to repress the side reactions.⁸¹ (Michaelis.)



The actual mechanism of the reaction is not known and may involve extensive disproportionation of intermediate products.

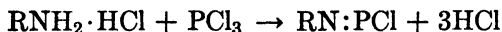
VII. Disproportionation of aryl amidophosphates

Diaryl N-dialkylamidophosphates readily disproportionate on heating and form mixtures of triaryl phosphates and the corresponding phosphoric triamides; the other by-products have not been identified. The reaction often occurs on attempted distillation of such products.⁷⁷

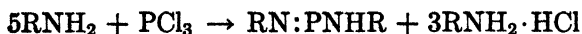


VIII. The reaction of primary aromatic amines or of their hydrochlorides with phosphorus trichloride

Prolonged heating of primary aromatic amine hydrochlorides with an excess of phosphorus trichloride results in a slow solution of the salts and the formation of N-arylimidochlorophosphites, which can be isolated by careful evaporation of the residual phosphorus trichloride.⁸⁹



Since the products react with amines (primary or secondary) and form the corresponding amido derivatives, RNHP:NR or $\text{R}_2\text{NP:NR}$, the preparation of the compounds of this category may be accomplished in a single operation in accordance with the equation proportions given below.⁴¹ (Grimmel *et al.*)

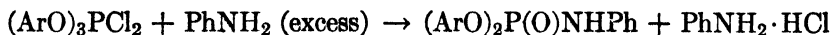


Usually the trichloride is added to the amine, which is dissolved in warm dry toluene, and the reaction is completed by refluxing for a brief period of time; generally 2 hours suffice. The by-product amine hydrochloride may be removed by filtration or by careful washing with cold water or alcohol.⁴¹ It may be noted that ortho- and paranitroanilines gave only tars in attempted syntheses of this type. In addition, it must be made clear that the products of the amidoimidophosphite structure are very reactive, and recrystallization from organic solvents often changes the structure of the originally obtained materials. The nature of such changes is not clear, but they are unmistakably shown in X-ray patterns. It is possible that these substances, ordinarily assumed to be dimeric,⁴¹ may undergo dissociation and association into more complex units, which would explain the X-ray pattern shifts.

IX. The reaction of phosphorus pentachloride with amines

Generally the reaction of primary and secondary amines with phosphorus pentachloride results in the formation of (N)-type quasi-phosphonium compounds. The reaction of the amine hydrochlorides, used in large excess, similarly yields the quaternary quasi-phosphonium derivatives (see Chapter 11). However, the intermediate products of such reaction mixtures may be utilized without isolation in a useful method of preparation of amidophosphates.

Thus the reaction mixture of an excess of a primary or secondary amine with phosphorus pentachloride, upon quenching with water, gives fair yields of the corresponding phosphoric amides.^{38, 64} The aryloxyphosphorus polyhalides, which may be obtained by the methods given in Chapter 11, and may be regarded as partially substituted phosphorus pentahalides, react with amines and form the corresponding esters of the amidophosphates. In such instances the reactions are conducted at mild temperatures, as a rule, similarly to the methods of Section II. However, radical displacement usually occurs, and the final products may contain fewer ester groups than the starting material. See example below.^{18, 133}



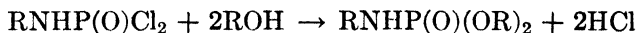
Refluxing secondary aliphatic amines with equimolar amounts of phosphorus pentachloride in chloroform yields not the expected N-type quasi-phosphonium compounds R_2NPCl_4 , but their adducts with an equivalent amount of the pentachloride (see Chapter 11).⁷⁷

Reaction of phosphorus pentachloride with aminobenzoic acids yields the amidodichlorophosphates of their acyl chlorides:^{77, 131}



X. Esterification of haloamidophosphates by hydroxy compounds or their sodium derivatives in anhydrous state

As a rule the direct esterification of the halides of amidophosphates by alcohols is not satisfactory. The relatively low reactivity of these halides, particularly the diamido derivatives, requires fairly high temperatures, which lead to disproportionation and other side reactions. Phenols can be made to react rather satisfactorily only at fairly high temperatures.⁷⁷ (Michaelis.)

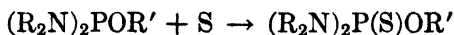
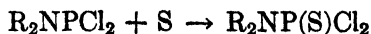


The use of pyridine in theoretically required amounts facilitates the reaction, and the esters can be produced fairly satisfactorily in dry inert solvents at moderate temperatures.^{8, 9, 10, 142} However, the usual destruction of the halide by the tertiary base takes place if the action is unduly prolonged (see Chapter 9). (Zetzsche; Audrieth.)

In a few instances the hydroxy compounds have been replaced by their sodium derivatives, RONa , which are used in the dry state in suspensions. As a rule, reactions of this type give better results than the direct action on the hydroxy compound, but they are not so satisfactory as the tertiary base.⁷⁷ Amidohalothionophosphates are so unreactive that the use of the sodium derivatives is imperative, and high temperatures for a prolonged period of time are necessary;⁷⁷ the yields are usually poor. The reactions given in Section II are preferred for the general synthesis of esters of the amidophosphates or amidothionophosphates.

XI. Reactions of the amidophosphites with sulfur

The amidophosphites based on trivalent phosphorus readily add one atomic equivalent of sulfur on being heated with this element, usually in a sealed tube, to temperatures in the vicinity of 100° . The halides are less reactive than the esters and require higher temperatures.⁷⁷ As a rule, some disproportionation of the ester and amide radicals may be encountered. (Michaelis.)



XII. The action of non-aqueous alkaline reagents on the halides

Reactions of this type are rather seldom used. Silver oxide is capable of dehydrohalogenating halodiamidophosphates based on primary amines with the resulting formation of amidoimidophosphates. Thus

the reaction with N,N' -diphenyl-diamidochlorophosphate yields N -phenylamido- N' -phenylimide.^{77, 78} (Michaelis.)



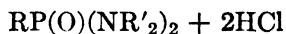
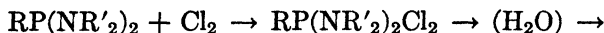
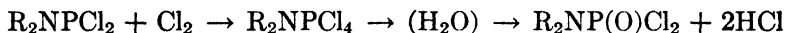
The alkaline decomposition of N -type quaternary quasi-phosphonium compounds yields triamidophosphates on moderate warming with alcoholic potassium hydroxide.⁷⁷



This reaction has been reported only for the amides of primary amines.

XIII. Addition of halogens (chlorine) to amidophosphites

In common with the other trivalent phosphorus derivatives, the amidohalophosphites, their neutral esters, and the amides of phosphonous acids readily add chlorine. As a rule, only the derivatives of secondary amines can be used because of the side reactions that take place at the NH group of the primary amine analogs.⁷⁷ The products can be readily converted to the corresponding amidophosphates or phosphonic acid derivatives by mild hydrolysis, usually exposure to moist air. As such, the intermediates usually belong to the quasi-phosphonium class of compounds, N -type. (Michaelis.)



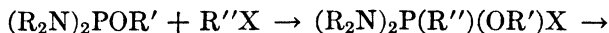
XIV. The action of sulfur dioxide on the polyhalides

The replacement of two chlorine atoms by a semipolar oxygen, shown in the previous section, can be accomplished by the use of water as indicated above. However, the reaction in this form usually gives a less clean-cut product than is obtainable from a similar replacement in which sulfur dioxide is used. This is a standard reaction for many polyhalides of phosphorus; it takes place at ordinary temperatures and the reaction products are readily isolated.⁷⁷ (Michaelis.)

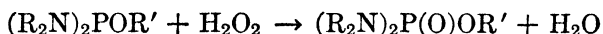


XV. The reaction of alkyl amidophosphites with alkyl halides

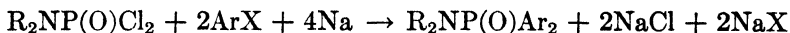
Ester amides of trivalent phosphorus react with alkyl halides (usually the more reactive iodides) upon heating and form the quaternary adducts, in a manner similar to the general action of esters of trivalent phosphorus (see Chapters 7 and 8). Action of water or heat serves to dissociate the adduct into an alkyl halide (radical of the original ester) and a phosphonamide.⁷⁷ (Michaelis.)

**XVI. Oxidation of amidophosphites**

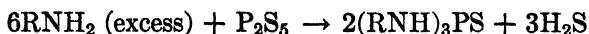
Although the reactions indicated in Sections XIII and XIV may be regarded as indirect oxidations of the amidophosphites, the direct oxidation has not found much practical application. Usually the esters of amidophosphites may be oxidized to the corresponding phosphates by the action of hydrogen peroxide at room temperature.⁷⁷

**XVII. The Würtz reaction of haloamidophosphates**

A number of aromatic phosphonamides have been prepared from aryl halides (chlorides or bromides) and chloroamidophosphates by an application of the Würtz reaction. The metallic sodium is added in lumps to the mixture of the reagents in an inert solvent (usually ether), and the suspension is gently warmed until the action subsides.⁷⁷ (Michaelis.)

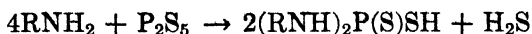
**XVIII. The reaction of primary and secondary amines with phosphorus pentasulfide**

A mixture of six moles of a primary amine with one mole of phosphorus pentasulfide yields, after heating for several hours to 180°, generally satisfactory amounts of thionophosphoric amides, which can be isolated after the conventional removal of the amine excess.²³ The secondary amines usually yield untractable oils. The aliphatic primary amines must be treated in sealed vessels because of the high temperatures necessary for the reaction.²³ (Buck *et al.*)



The actual yields generally are in the vicinity of 50%. This reaction is in fact a continuation of the primary reaction, in which four moles

of the amine react at substantially room temperature with one mole of the pentasulfide and yield the corresponding diamidodithiophosphate. The products may be isolated by careful extraction with cold alkali and precipitation by cold dilute hydrochloric acid. The action of warm aqueous reagents in contact with air is oxidative and should be avoided.²³



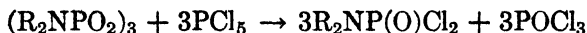
There is little question that the above equation is only a crude overall representation, for the action of the amine undoubtedly proceeds by a stepwise attack upon the monolithic structure of an actual aggregate of the "pentasulfide," which is a multiple of the simple formula given above.

XVIII. The reaction of diamidodithiophosphates with amines. As indicated above, the formation of triamidothionophosphates from phosphorus pentasulfide is a two-step process. The second step may be carried out separately by heating the diamidodithiophosphate with the amine to approximately 180°. The yields are only fair.



XIX. The reaction of N-dialkylamidometaphosphates with phosphorus pentachloride

Heating N-dialkylamidometaphosphates with phosphorus pentachloride, generally in moderate excess, results in a fairly satisfactory yield of the corresponding N-dialkylamidodichlorophosphate. The action is essentially a progressive cleavage of the phosphorus to oxygen to phosphorus bonds in the cyclic aggregate of the meta derivative.⁷⁷



XIXA. Ammonolysis of dialkylamidometaphosphates. A useful form of cleavage of the meta derivatives takes place in the reaction with alcoholic solutions of ammonia. Presumably the action proceeds by a progressive ammonolytic attack on the phosphorus to oxygen to phosphorus bonds of the cyclic meta derivative.⁷⁷

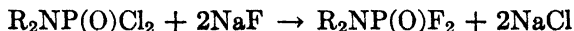


The formulation given above appears to be reasonable, but the work has not been checked by subsequent investigators and may bear repetition. The use of amines instead of ammonia has not been investigated.

XX. Metathetic exchanges in the haloamidophosphates

The exchange of the chlorine atoms in N-dialkyldichloroamidophosphates by fluorine can be accomplished by warming with sodium

fluoride in dry benzene.^{19, 49} Exchange for the cyano or thiocyno derivatives may be made similarly by the use of potassium salts.



Similar exchanges can be performed with the analogous diamido derivatives. The stability of these permits the use of aqueous solutions of potassium fluoride,¹⁹ or the use of hydrogen fluoride with antimony trifluoride catalyst.⁴⁹

XXI. The reaction of acid amides with phosphorus pentachloride

The action of phosphorus pentachloride on the amides of carboxylic acids yields, as primary products, substances of the general type $\text{RCCl}:\text{NP}(\text{O})\text{Cl}_2$. These can be isolated after the equimolar mixture has been warmed to about 50°. The actual isolation succeeds well with derivatives of acetamides, which contain appreciable negative substitution in the acid radical.^{22, 123, 130, 134} Exposure to moist air results in the hydration of such products with the formation of the acyl derivatives, $\text{RCO} \cdot \text{NHP}(\text{O})\text{Cl}_2$. The exposure to moisture must be limited if the complete cleavage of the product is to be avoided. The unsubstituted amides usually defy isolation.

XXII. The action of phosphorus pentachloride on salts of diamidophosphates

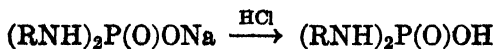
The applications of this reaction have been too few in number for its scope to be determined. A few diamidophosphates of the aryl series have been converted to the corresponding chlorophosphates.



XXIII. Hydrolysis of amidochlorophosphates

Usually the ordinary hydrolytic treatment of the amidochlorophosphates by water or acids results in complete decomposition. The derivatives of the secondary amines are somewhat more stable than those of the primary amines, in this respect; aryl derivatives also supersede the alkyls.

However, careful addition of diamidochlorophosphates to cold aqueous sodium carbonate, followed by careful acidification, yields the corresponding free acids:^{26, 77}

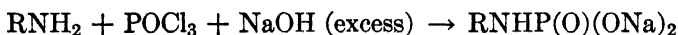


The monoamidodichlorophosphates have not been investigated thoroughly in this respect. It has been reported that careful addition of N-arylamidodichlorophosphates to cold ammonium hydroxide, followed by careful acidification, yields the corresponding N-aryldiamidophosphates, shown by the formula $(\text{RNH})\text{P}(\text{O})(\text{NH}_2)\text{OH}$.^{26,77} However, the analyses of the reported products correspond more closely to the monoammonium salts of monoamide.

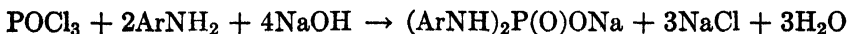
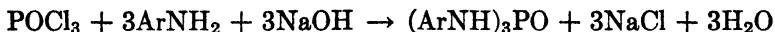
XXIV. The Schotten-Baumann reactions of the chlorophosphates

In the simplest form of this reaction, aliphatic amines, principally amino acids, have been phosphorylated by addition of phosphorus oxychloride to their aqueous solutions containing magnesium oxide suspensions. The products were not correctly characterized, since in the case of hydroxyamino acids, the phosphorylation occurred at both active groups.^{99,137}

Somewhat better results, although with moderate actual yields, were obtained by the use of fairly concentrated cold sodium hydroxide (usually 17 N). After the removal of the phosphate ion, mostly in the form of trisodium phosphate with the "clean-up" by precipitation of magnesium ammonium phosphate in dilute ammoniacal solution, the products were isolated in the form of salts, calcium or barium.^{99,137,140} (Zeile *et al.*)



An extensive study of such reactions with primary aromatic amines showed that the synthesis of phosphoric amides and diamidophosphates could be accomplished quite successfully at room temperature, or somewhat below, provided that an excess of the alkali was constantly present.^{11,16} Usually, 10% sodium hydroxide favors the diamido derivative formation; a 25% solution (or higher) increases the yield of the triamides.

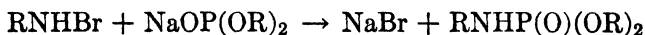


The products are separated by virtue of the solubility of the diamidophosphates, as acids, in the alkaline solution.¹⁶ For best results an equimolar ratio of the amine and the oxychloride is advised. Thiophosphoryl chloride reacts similarly and yields similar thionotriamides, $(\text{ArNH})_3\text{PS}$, and the salts of diamidothiophosphates, $(\text{ArNH})_2\text{POSNa}$.¹⁶

Obviously, chlorophosphates in general can be used in such reactions; usually the aryl esters only are employable because of the hydrolyzability of the alkyl derivatives. The aryl chlorothionophosphates react satisfactorily with ammonium hydroxide, as a rule, but their reactions with aromatic amines require the Schotten-Baumann conditions.¹⁴ As a rule, the use of 10% alkali leads to the formation of a mixture of all possible products, and the aryl dichlorothionophosphates yield the aryl N,N'-diaryldiamidothiophosphates, $(\text{RO})\text{P}(\text{S})(\text{NHR})_2$, small amounts of the haloamido derivatives, $(\text{RO})(\text{RNH})\text{P}(\text{S})\text{Cl}$, and the salts of the free acids of the latter type.¹⁵ Acidification of the alkaline filtrate from such reaction mixture gives, according to Autenrieth,¹⁵ a precipitate of an "ortho" diamidophosphate that has been assigned the formulation $(\text{RO})(\text{RNH})_2\text{P}(\text{SH})(\text{OH})$. Such acids reportedly lose hydrogen sulfide on heating in mineral acids, or on heating, and yield the normal diamido derivatives $(\text{RO})(\text{RNH})_2\text{PO}$. Oxidation of the sodium salts of such ortho acids by iodine yields neutral disulfides with a loss of a molecule of the amine per each molecule of the salt. The disulfides, $(\text{RO})(\text{RNH})\text{P}(\text{O})\text{SSP}(\text{O})(\text{NHR})(\text{OR})$, resemble the phosphatogens of type $(\text{RO})_2\text{P}(\text{O})\text{S}\cdot\text{SP}(\text{O})(\text{OR})_2$ (see Chapters 8 and 9). The true structure of the ortho acids has not been established.

XXV. The reactions of N-bromo compounds with dialkyl sodium phosphites

Several N-phosphorylated amino acids have been prepared by the reaction of their N-halo derivatives with diethyl sodium phosphite. The details of the procedures are lacking, but the reaction may be presumed to proceed in inert solvents in accord with ⁷ (Aubel, Reich),



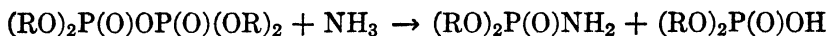
XXVI. Ammonolysis of phosphates or thionophosphates

The possibility of the formation of amidophosphates by interaction of esters with ammonia or with amines has not been explored adequately. The few items of information available are contradictory, thus making a definitive statement an impossibility.

Although triethyl phosphate was reported to be unaffected by dry ammonia at 160°, ¹²⁶ another report claims the synthesis of diethyl amido phosphate from either triethyl phosphate or triethyl thionophosphate by heating with ammonia in ether or alcohol solutions to temperatures in the vicinity of 130 to 140°. ¹⁰³ The analysis of the reported product is in perfect agreement with theory, but the melting point is far from that of the preparations of this substance by other methods.

A few recent investigations of the subject appear to indicate that amidation by such means does not lead to success and that alkylation of the amine usually occurs instead (see Chapter 9). However, the patent literature contains claims of such displacements of the ester groups in aryl phosphates (or phosphites) by primary amines, with the formation of mixtures of diaryl amidophosphates and aryl diamidophosphates. Catalysis by alkaline reagents and sodium alkoxides is said to be effective.³⁵

Ammonolysis of the phosphorus to oxygen to phosphorus bonds in esters of condensed phosphoric acid is likely to form amidophosphates, however. The tetraesters of pyrophosphoric acid form the expected amidophosphates.⁶

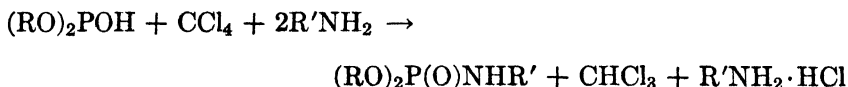


The alkyl metaphosphates, $(\text{ROPO}_2)_x$, do not present a clear picture at this time. The originally claimed formation of amidophosphates from them and the amines, or ammonia,⁶¹ appears to have been upset by more recent studies,¹⁰⁴ in which only the amine salts were obtained, although the patent literature still refers to amide formation in such cases.¹³⁸ The reaction of primary amines with tetra-alkyl hypophosphates, which are customarily represented as $(\text{RO})_2\text{P}(\text{O})\text{OP}(\text{OR})_2$, results in the formation of crystalline substances, which, however, are not amidophosphates. They are isomeric with the amidophosphates of formula $(\text{RO})_2\text{P}(\text{O})\text{NHR}'$, but they are acidic substances rather than neutral.² They have been assigned a provisional formulation $(\text{RO})_2\text{P}(\text{OH})\text{:NR}$; it is possible that they are hydrogen-bonded adducts to the dialkyl phosphite ions. The patent literature also claims the formation of mixtures of imido- and amidophosphites by heating amine salts of phosphorous acid to 180° ; ¹¹⁶ a verification of the products appears to be necessary.

XXVII. The reaction of secondary phosphites with amines in the presence of a polyhalo compound

Secondary phosphites, $(\text{RO})_2\text{POH}$, react smoothly with primary or secondary amines in the presence of an aliphatic polyhalide and form amidophosphates in usually excellent yields. Although carbon tetrachloride has been the customary reagent, other polyhalides may be used. Carbon tetrabromide, carbon trichlorobromide (most effective), iodoform, bromoform, dichlorobromoethane, sym-tetrachlorodibromoethane, pentachloroethane, and hexachloroethane have been used; fluorinated compounds are generally poor.^{5,6} The actual mechanism of the reaction is not clear; intermediates of the types $(\text{RO})_2\text{P}(\text{O})\text{X}$ or

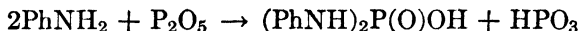
$(\text{RO})_2\text{P}(\text{O})\text{CX}_3$ may be postulated. The former are, of course, chlorophosphates, which would be expected to yield the amidophosphates with the amines. However, the compounds of the latter type have been isolated (see Chapter 7) and have been shown to yield identical amidophosphates. Usually, diethyl or the dibenzyl esters are used for high-yield reactions. With carbon tetrachloride reagent it is possible to obtain good reaction with the aliphatic amines but not with the aromatic ones, like aniline, unless an auxiliary tertiary base is present (dimethylcyclohexylamine, usually), but the bromo compounds are sufficiently active to react per se without the tertiary base.⁵ An example of a typical reaction is shown below. (Todd.)



XXVIII. The reaction of phosphorus pentoxide with amines

Heating phosphorus pentoxide in toluene suspension with four moles of aniline for several hours yields minute amounts (5 to 6%) of the corresponding diamidophosphate, $(\text{PhNH})_2\text{P}(\text{O})\text{OH}$. The main product is the amine salt of metaphosphoric acid. These results are in accord with the results obtained with alkyl metaphosphates (Section XXVI).²⁵

The simple formulation of the reaction in the form of



is obviously insufficient; the true picture must show the progressive attack on the phosphorus-oxygen-phosphorus bond network in the monolithic structure of the oxide. The instability of the mono- and diamides is undoubtedly the contributing factor to the poor yield of an amidophosphate. In great contrast, provided by the alcohol-pentoxide reaction, the acidic esters formed in the esterification are stable at the relatively low temperatures that suffice for reaction. Except for the stability of the primary products, the two reactions are probably very nearly identical.

XXIX. Reactions of phosphoric imidoamides

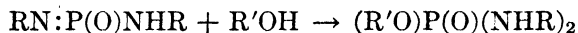
The substances belonging to this general category may be assigned a class formula of a monomer $\text{RN}:\text{P}(\text{O})\text{NHR}$, for their reactions, which are listed below, may be readily explained by additions to the imide structure. The usually observed dimeric molecular weight does not preclude dissociation in reactions, and indeed boiling point methods give an indication of such dissociation.

Reactions, usually at reflux temperatures or in sealed tubes for the lower boiling members, with primary amines lead to the corresponding phosphoric amides.^{26, 77, 78} (Michaelis.)

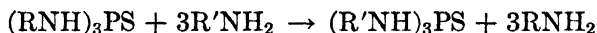


If aliphatic amines are used with the aniline derivative, the products are not mixed phosphoric amides. Some triphenyltriamide is obtained along with unidentified products that may contain some mixed triamides. A positive identification of these would be of great interest.²⁵

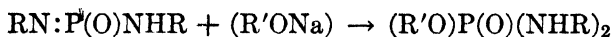
Similar reactions with phenols lead to aryl diamidophosphates.⁷⁷



The reaction of the amines, shown above, is also operative with the amidoimidothiono derivatives, RN:P(S)NHR . Mixed derivatives could not be obtained in this reaction. However, a simplified version of the reaction, which probably goes via the imido derivatives, is obtained if the thionophosphoric amide is heated to 150 to 180° with a primary amine. In this case only symmetric thionosphoric amides were obtained, in which an apparent transposition of the radicals took place. The mixtures of the different triamides, as a rule, were not resolved, and the high level of uncrystallizable residues obtained did not preclude the formation of some mixed derivatives. The usual representation of this over-all reaction may be shown as ²⁴ (Buck *et al.*)



XXIXA. The reaction of amidoimidophosphates with sodium alkoxides. The phosphoric imidoamides react with sodium alkoxides, in solution in the corresponding alcohol, and form the esters of the diamidophosphates.⁷⁸ (Michaelis.)



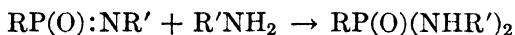
The reactions with dry sodium phenoxide yield products that have been identified only tentatively as amides of imidophosphoric acids.⁷⁸

XXX. Oxidation of amidothionophosphates

Although phosphoric amides are quite resistant to hydrolytic and oxidative attack, their thiono analogs may be expected to undergo a more or less ready oxidation to the PO analogs. Thus tri-2-naphthylthionophosphoric amide was oxidized to the corresponding phosphoric triamide in the course of a usual recrystallization.²³ Little precise information is available about reactions of this type.

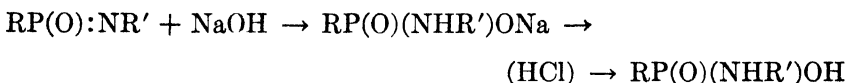
XXXI. Reactions of phosphonimides

The imides of phosphonic acids, RP(O):NR , undergo reactions that are essentially duplicated by the phosphoric imides (Section XIX). This set of reactions may be illustrated by the formation of phosphonodiamides, from these substances, upon heating with primary amines.⁷⁸

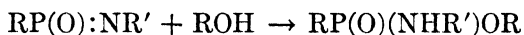


If the second amine is different, mixed amides may be secured.⁷⁸ Secondary amines react rather sluggishly in a similar reaction.⁷⁸ (Michaelis.)

Mild hydrolysis by warm sodium hydroxide solutions yields the phosphonomoamides, which can be recovered from the alkaline solution by careful acidification.⁷⁸



Brief heating with alcohols or phenols yields the esters of the monoamides.⁷⁸

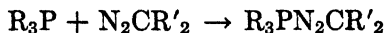
**XXXII. Preparation of phosphinimines and related compounds**

Tertiary phosphines react with organic azides in the formation of adducts, $\text{R}_3\text{P} \rightarrow \text{N}_3\text{R}'$, the precise structure of which is unknown. As a rule, these substances are poorly stable and decompose on warming with loss of nitrogen molecule and the consequent formation of semipolarly linked phosphinimines.¹¹⁹⁻¹²² (Staudinger *et al.*)



The aliphatic members may be distilled for isolation; the aryl derivatives are crystallizable.

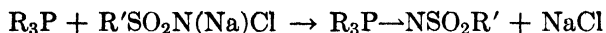
In a similar manner, tertiary phosphines add diazo compounds and form so-called phosphazines.¹¹⁹⁻²² The compounds are usually crystalline solids easily recoverable from the reaction mixtures, provided that hydrolysis is avoided.



There are insufficient data to assign the mode of phosphorus to nitrogen link in these substances. The link, however, is rather easily cleaved by hydrolytic means and may be semipolar.

A rather unusual formation of phosphinimines takes place in the reaction of tertiary phosphines with Chloramine-T. If a dry reagent is

used, true phosphinimines are formed, which are based on the toluene-sulfonamide radical. (Mann *et al.*)



Hydrated chloramine, however, may yield either the phosphinimines or their hydrates (probably quasi-phosphonium hydroxides), depending upon the polarity of the semipolar bond in the phosphinimine. Reduced polarity, which obtains upon ortho or para substitution in the phenyl radicals of a triaryl phosphine by methyl, methoxy, or chlorine radicals, leads to the phosphinimines to a substantial extent, with para substitution being less effective. In a corollary reaction a few triarylphosphine oxides react with anhydrous chloramine and yield similar products. The reaction is shown only by the oxides that have a high order of polarity in their phosphoryl group.⁷¹

XXXIII. Miscellaneous reactions

The organic reactions of phosphonitrilic chlorides, $(PNCI_2)_n$, have been explored too incompletely up to this date to be worth considering. Phenylation of the trimer and the tetramer by phenylmagnesium bromide, or less effectively by the Friedel-Crafts methods, yields a mixture of derivatives that indicate significant monomeric dissociation in their reactions.^{20, 21} A few apparently monomeric amides, $NP(NHR)_2$, have been prepared by amine interaction,¹⁰⁸ with benzylamine yielding only partially amidated product.¹¹²

The reaction of aliphatic nitriles with phosphorus pentasulfide has been reported to take place at about 100°. The nature of the products is unknown, but they may be expected to be phosphorus-nitrogen linked derivatives.^{106, 117}

The reaction of phosphorus oxychloride with N-arylanthranilic acids or N-substituted acridones yields rather unstable intermediates that exist as ionic substances having dichlorophosphate anion.^{39, 40}

GENERAL CHARACTERISTICS

The haloamidophosphates, as a class, may be regarded as the acid halides of the family of amidophosphates. Their acid chloride character is very significantly suppressed by the amido groups, however. This becomes very apparent in the pure substances, obtainable from the "crudes" by a very long evacuation that removes traces of residual hydrogen halides. The purified substances enter the usual reactions quite sluggishly. Thus even the dichloro derivatives may be dissolved in cold dilute carbonates and recovered unchanged upon acidification

in the cold.²⁶ The halodiamido derivatives have even less of the acid halide character.

The triamido derivatives are in many respects the most stable substances in this family. Usually they can withstand rather drastic hydrolytic media, both acid and alkaline. The behavior of their thiono analogs has been mentioned earlier.

All, even the triamides, however can be hydrolyzed to phosphoric acid by sufficiently drastic methods.

The phosphoryl group in the triamides or in ester amides, as well as PS in the corresponding thiono compounds, displays a pronounced hydrogen bonding tendency, in a manner similar to that shown by the phosphate esters. The tendency is strikingly shown in the amides of secondary amines, in which the internal bonding via the NH-PO group does not take place. The solubilities of such compounds are remarkable even in substances of large molecular weights.¹⁰ These substances should be of much interest as plasticizers.

Perhaps the most spectacular property in this family is the high level of toxicity displayed by the diamidofluorophosphates of secondary amines, in many ways similar to that of the secondary fluorophosphates.^{19, 44, 68} These substances, incidentally, are quite resistant to mild hydrolysis.⁴⁴

Although the intrafamily reactions are representatively shown in the sections devoted to the synthetic methods, several reactions that lead to other types of compounds may be mentioned.

Alkyl N-dialkylamidochlorophosphates, $(RO)P(O)(NR_2)Cl$, and to a lesser degree the corresponding phosphites, react on heating, or even upon attempted distillation, and form N-dialkylamidometaphosphates (see Chapter 12).⁷⁷ The tetra-alkyl diamidochlorophosphates react with the corresponding ester amides and form the tetra-amides of the pyrophosphate series (Chapter 12).¹⁹

Phosphoric imidoamides react with carboxylic acids and form the amides of the acids.⁴¹ Similarly, imidochlorophosphites yield acyl chlorides and amides of carboxylic acids.⁴¹

The phosphinimines and related compounds are readily hydrolyzed to the corresponding phosphine oxides, thus confirming the semipolarity of the phosphorus-nitrogen link in these substances. Even the so-called phosphazines, $R_3PN_3CR'_2$, can be best regarded as coordination compounds, for they are readily dissociated in solutions.¹⁷

The amidophosphates and their thiono analogs are as a rule crystalline substances, especially when derived from the arylamines. The derivatives of dialkylamines, however, are frequently liquids with quite low boiling points. This property is undoubtedly connected with the

absence of intermolecular hydrogen bonding, mentioned earlier. Many of the rather interesting reactions used in the synthesis and the interconversions in this family are very imperfectly understood. For this reason a considerable degree of confusion exists in the literature on this subject to the present day. The elimination of such confusion is extremely necessary, and its accomplishment is one of the greater challenges in the field of organophosphorus compounds.

COMPOUNDS WITH PHOSPHORUS TO NITROGEN BONDS

A. COMPOUNDS WITH PHOSPHORUS TO HALOGEN BOND

1. HALOPHOSPHITES

- EtNHPCl₂**. I. Liquid, b. 222–5°, b₁₁ 92°.⁷⁷
PrNHPCl₂. I. Liquid, b₁₀ 97°, d₀¹⁵ 1.226.⁷⁷
iso-BuNHPCl₂. I. Liquid, b₁₀ 101°, d₀¹⁵ 1.213.⁷⁷
AmNHPCl₂. I. Liquid, b₈ 101°.⁷⁷
Et₂NPF₂. XX. Gas.⁴⁹
Et₂NPCl₂. I.^{49,77} Liquid, b. 189°, b₁₄ 72–5°, d₀¹⁵ 1.196.⁷⁷
Pr₂NPCl₂. I. Liquid, b₁₁ 95°, b. 220–3°.⁷⁷
iso-Bu₂NHPCl₂. I. Crystals, m. 37–8°, b₁₀ 116–7°.⁷⁷
iso-Am₂NPCl₂. I. Liquid, b₈ 140°.⁷⁷
C₆H₁₀NPCl₂. I. Liquid, b₁₀ 94–5°.⁷⁷
Et₂NP(OEt)Cl. I. Liquid, b₁₃ 90–2°.⁷⁷
C₆H₁₀NP(OEt)Cl. I. Liquid, b₂₅ 125°.⁷⁷
MePhNPCl₂. I. Liquid, b. 251°, b₁₀ 138–40°.⁷⁷
EtPhNPCl₂. I. Liquid, b₁₂ 143°.⁷⁷

2. HALOPHOSPHATES

A. DIHALOPHOSPHATES

i. DERIVATIVES OF PRIMARY AMINES

- MeNHPOCl₂**. III. Liquid, b₂₇ 132°.⁷⁷
EtNHPOCl₂. III. Liquid, b₂₂ 140°.⁷⁷
PrNHPOCl₂. III. Liquid, b₁₆ 146°.⁷⁷
iso-BuNHPOCl₂. III. Liquid, b₁₄ 141°.⁷⁷
AmNHPOCl₂. III. Liquid, b₁₇ 159°.⁷⁷
PhCH₂NHPOCl₂. II. Undistillable oil.⁷⁷
PhNHPOCl₂. II.²⁶ III.^{12,77,90} Needles (from benzene-ligroin), m. 93–4°,²⁶ m. 87° (from CCl₄).¹⁴⁸ m. 84°.^{12,77,90}
4-ClC₆H₄NHPOCl₂. III.¹⁰¹ Needles, m. 107° (from benzene).^{77,101}
2,4-Cl₂C₆H₃NHPOCl₂. III. Needles, m. 126° (from benzene-ligroin).⁷⁷
2,4,6-Cl₃C₆H₂NHPOCl₂. II. Crystals, m. 128° (from benzene-ligroin).⁷⁷
4-BrC₆H₄NHPOCl₂. III. Rods, m. 98° (from benzene-ligroin).⁷⁷
3-BrC₆H₄NHPOCl₂. III. Crystals, m. 87°.⁷⁷
2,4-Br₂C₆H₃NHPOCl₂. III. Crystals, m. 134°.⁷⁷
2,4,6-Br₃C₆H₂NHPOCl₂. II. Needles, m. 148°.⁷⁷
3-O₂NC₆H₄NHPOCl₂. III. Needles, m. 148°.⁷⁷
4-O₂NC₆H₄NHPOCl₂. III. Needles, m. 156°.⁷⁷
2-MeC₆H₄NHPOCl₂. III.⁹¹ Crystals, m. 91° (from benzene).^{77,90,91}

- 4-MeC₆H₄NHPOCl₂**. II.²⁶ III.^{77, 90} Rhombic crystals, m. 110–1° (from benzene-ligroin),²⁶ m. 104°.^{77, 90}
2-Br-4-MeC₆H₃NHPOCl₂. III. Scales (from benzene-ligroin).⁷⁷
2,4-Me₂C₆H₃NHPOCl₂. II. III. Needles, m. 79° (from ligroin).⁷⁷
2,5-Me₂C₆H₃NHPOCl₂. II. III. Needles, m. 119°.⁷⁷
3,4-Me₂C₆H₃NHPOCl₂. II. III. Needles, m. 76°.⁷⁷
1,2,4-Me₃C₆H₂NHPOCl₂. II. III. Crystals, m. 122°.⁷⁷
3-ClCO·C₆H₄NHPOCl₂. IX. Prisms, m. 109–10° (from CHCl₃).⁷⁷
4-ClCO·C₆H₄NHPOCl₂. IX. Prisms, m. 168° (from CHCl₃).⁷⁷
2-ClCO·C₆H₄NHPOCl₂. IX (poor yield).¹²¹ Prisms, m. 62° (from ligroin).¹²¹
4-H₂N·SO₂·C₆H₄NMe(POCl₂). II. Powder.⁴⁸
4-(Cl₂PO·NHC₆H₄)₂SO₂. II. Crystalline solid.⁵⁰
5-(4-Hydroxy-2-ethylmercapto-5-imino)pyrimidyl dichlorophosphate. II. Crystals, dec. 247–50°.⁵¹

ii. DERIVATIVES OF AMIDES

- ClCH₂·CCl:NPOCl₂**. XXI. Liquid,¹²³ b_{0.2} 100°.²²
ClCH₂·CO·NHPOCl₂. By action of moisture on above compound. Crystals (from benzene).¹²³
BrCH₂·CCl:NPOCl₂. XXI. Crude oil.¹²³
Cl₂CH·CCl:NPOCl₂. XXI. Crystals,¹³⁴ b_{0.3} 92–4°, m. 39°.²²
Cl₂CH·CO·NHPOCl₂. By action of moisture on above compound. Plates, m. 113°,²² m. 112–3° (from benzene).^{123, 124}
Cl₃C·CCl:NPOCl₂. XXI. Plates, b. 255–9°,¹³⁴ b₁₁ 140°,²² m. 80°,²² m. 78–81°.¹³
Cl₃C·CO·NHPOCl₂. By action of moisture on the above compound. Needles⁴ m. 146–8° (from ligroin).^{123, 124}
ClHBrC·CCl:NPOCl₂. XXI. Yellow oil.¹²³
ClBrCH·CO·NHPOCl₂. By action of moisture on above compound. Crystals.¹²³
Cl₂BrC·CCl:NPOCl₂. XXI. Crystals, m. 68°.¹²³
Cl₂BrC·CO·NHPOCl₂. By action of moisture on above compound. Crystals, m. 147° (from ligroin).^{123, 124}
Br₃C·CCl:NPOCl₂. XXI. Liquid, which freezes on standing.¹²³
Br₃C·CO·NHPOCl₂. By action of moisture on the above compound. Crystals, m. 105–6° (from benzene).^{123, 124}
Cl₂(O₂N)C·CCl:NPOCl₂. XXI. Crystals, m. 55–60°.¹²³
Cl₂(O₂N)C·CO·NHPOCl₂. By action of moisture on the above compound. Crystals, dec. 165° (from benzene).^{123, 124}
Br₂(O₂N)C·CCl:NPOCl₂. XXI. Crystals, m. 65°.¹²³
Br₂(O₂N)C·CO·NHPOCl₂. By action of moisture on the above compound. Crystals, dec. 187–8°.^{123, 124}
MeCCl₂·CCl:NPOCl₂. XXI. Needles, m. 80° (from ligroin).¹²³
MeCCl₂·CO·NHPOCl₂. By action of moisture on the above compound. Needles, m. 127–8° (from benzene).¹²³
(EtO₂C)·CCl₂·NHPOCl₂. XXI (by-product). Crystals, m. 128–30° (from CHCl₃).¹³⁴
PhBrCH·CCl:NPOCl₂. XXI. Liquid.¹²³
Ph₂ClC·CCl:NPOCl₂. XXI. Liquid.¹²³
Ph₂ClC·CO·NHPOCl₂. By action of moisture on the above compound. Crystals, m. 122–3°.^{123, 124}

302 COMPOUNDS WITH PHOSPHORUS TO NITROGEN BONDS

PhCO·NHPOCl₂. XXI, followed by action of moisture. Plates, m. 115° (on rapid heating), dec. 110° (on slow heating).¹³⁰

Ph·SO₂·NHPOCl₂(?). XXI. Crystals, m. 130–1°. ^{77,138}

iii. DERIVATIVES OF SECONDARY AMINES

Me₂NPOF₂. XX. Liquid, b₁₀ 28°. ¹⁹

Me₂NPOCl₂. III. Liquid, b. 194–5°, b₂₂ 90–1°. ⁷⁷

Et₂NPOF₂. XX. Liquid, b₁₈ 45–6°. ⁴⁹

Et₂NPOCl₂. II. ⁷⁷ III. ⁷⁷ Liquid, b. 220°, b₁₅ 100°, ⁷⁷ b₁₅ 99°. ⁴⁹

Et₂NPOBr₂. II. Undistillable oil. ⁷⁷

Pr₂NPOCl₂. II. III. XIII. Liquid, b. 243–4°, b₂₀ 123°. ⁷⁷

Pr₂NPOBr₂. II. Undistillable oil. ⁷⁷

iso-Bu₂NPOCl₂. II. XIII. Crystals, m. 54° (from EtOH). ⁷⁷

iso-Bu₂NPOBr₂. II. Needles, m. 68°. ⁷⁷

iso-Am₂NPOCl₂. II. Liquid, b₁₂ 150°, d₀¹⁸ 1.0804. ^{77,84}

PhMeNPOCl₂. II. III. Liquid, b. 282°, b₁₀ 150–1°. ⁷⁷

PhEtNPOCl₂. II. III. Liquid, b₁₈ 159°. ⁷⁷

Ph₂NPOCl₂. II. Plates, m. 57° (from ligroin). ^{77,101}

C₆H₁₀NPOCl₂. III. Liquid, b. 257°, b₁₁ 124°, d₀¹⁸ 1.323. ⁷⁷

C₉H₁₀NPOCl. II (from tetrahydroquinoline). Needles, m. 79°. ⁷⁷

B. MONOHALOPHOSPHATES

i. DERIVATIVES OF PRIMARY AMINES

(EtNH)₂POCl. II. Needles, m. 74° (from Et₂O). ⁷⁸

(PrNH)₂POCl. II. Needles, m. 88° (from benzene-ligroin). ⁷⁷

(BuNH)₂POCl. Not isolated.

(BuNH)₂POF. II. Needles, m. 59.5° (from ligroin), b_{2.5} 177°. ⁴⁴

(iso-BuNH)₂POCl. II. Needles, m. 86°. ⁷⁷

(C₆H₁₁NH)₂POF. II. Needles, m. 127° (from dil. EtOH). ⁴⁴

(PhNH)₂POF. II. Needles, m. 145° (from dil. EtOH). Soluble in hot water. ⁴⁴

(PhNH)₂POCl. III. ^{77, 91, 92, 142} XXII. ¹⁶ Needles, m. 176°, ¹⁴² m. 174°, ^{77, 92} m. 171–2° (from xylene), ¹⁰⁰ m. 159° (from dil. EtOH). ¹⁶

(4-ClC₆H₄NH)₂POCl. III. Crude waxy solid. ¹⁰¹

(PhCH₂NH)₂POF. II. Crystals, m. 96° (from 90% EtOH). ⁴⁴

(2-MeC₆H₄NH)₂POCl. III. Needles, m. 190°. ^{77, 91}

(PhNH)(4-MeC₆H₄NH)POCl. II. Needles, m. 133–4° (from benzene). ⁸⁶

(4-MeC₆H₄NH)₂POCl. III. Needles, m. 210°. ^{77, 91}

(PhNH)(PhCO·NH)POCl. II (from PhCONHPOCl₂). Needles, m. 176° (from EtOH). ¹³⁰

ii. DERIVATIVES OF SECONDARY AMINES

(Me₂N)(MeNH)POF. Liquid, b₃ 110°. ¹⁹

(Me₂N)₂POF. II. ^{19, 44} XX. ¹⁹ Liquid, b₁₇ 96°, ¹⁹ b₁₅ 86°, ⁴⁴ b₁₀ 86°, b₆ 69–70°, b₄ 67°, ¹⁹ d₄²⁵ 1.1. ⁴⁴

(Me₂N)(MeEtN)POF. Liquid, b₁₁ 90°. ¹⁹

(MeEtN)₂POF. Liquid, b₉ 105°. ¹⁹

(Me₂N)(Et₂N)POF. Liquid, b₁₀ 102°. ¹⁹

(Et₂N)₂POF. Liquid, b₈ 113°. ¹⁹ II. Liquid, b₂₀ 124.5–5.5°, b₂₃ 127–8°. ⁴⁴

(MePhN)(MePhN)POF. Liquid, b₈ 77°. ¹⁹

(MePhN)₂POF. II. Liquid, b_{0.08} 163–5°. ⁴⁴

- (Me₂N)(EtPhN)POF.** Liquid, *b*₄ 110–5°. ¹⁹
(EtPhN)(PhNH)POCl. II. Prisms, *m.* 113° (from CHCl₃). ⁷⁷
(O(CH₂CH₂)₂N)₂POF. II. Crystals, *m.* 40°; hygroscopic. ⁴⁴
(C₆H₁₀N)₂POF. II. Liquid, *b*_{0,3} 145°. ⁴⁴
(C₆H₁₀N)₂POCl. II. Liquid, *b*₁₂ 184°. ⁷⁷
(C₆H₁₀N)(PhNH)POCl. II. Needles, *m.* 174–5°. ⁷⁷
(C₆H₁₀N)(2-MeC₆H₄NH)POCl. II. Crystals, *m.* 122°. ⁷⁷

iii. DERIVATIVES WITH AN ESTER FUNCTION

- Me₂NPO(OCH₂CH₂Cl)F.** X–XX. Liquid, *b*₈ 69°. ¹⁹
Et₂NPO(OEt)Cl. II. XIX. Liquid, *b*₁₈ 113°. ⁷⁷
Pr₂NPO(OEt)Cl. II. Liquid, *b*₁₀ 240° (with decomposition). ⁷⁷
iso-Bu₂NPO(OEt)Cl. II. Undistillable liquid. ⁷⁷
PhNHPO(OMe)Cl. II. Needles, *m.* 82–3° (from ligroin). ²⁶
PhNHPO(OEt)Cl. II. Pyramidal crystals, *m.* 61–2°. ²⁶
PhNHPO(OPh)Cl. II. III. X. Needles, *m.* 137° (from benzene). ⁷⁷
4-MeC₆H₄NHPO(OMe)Cl. II. Prisms, *m.* 115–6° (from benzene). ²⁶
4-MeC₆H₄NHPO(OEt)Cl. II. Prisms, *m.* 74–5°. ²⁶
4-MeC₆H₄NHPO(OPh)Cl. Crystals (II), *m.* 77° (from benzene-ligroin). ⁷⁷

3. HALOTHIONOPHOSPHATES

A. DIHALOTHIONOPHOSPHATES

i. DERIVATIVES OF PRIMARY AMINES

- MeNHPSCl₂.** IV. V. Liquid, *b*₃₃ 115°. ⁷⁷
EtNHPSCl₂. IV. V. Liquid, *b.* 216°, *b*₉ 105°, *b*₂₀ 115°. ⁷⁷
PrNHPSCl₂. V. Liquid, *b*₁₇ 121°. ⁷⁷
iso-BuNHPSCl₂. IV. V. Liquid, *b.* 251°, *b*₁₅ 123°, *b*₉ 116°. ⁷⁷
AmNHPSCl₂. V. Liquid, *b*₁₆ 140°. ⁷⁷
PhCH₂NHPSCl₂. IV. Undistillable oil. ⁷⁷

ii. DERIVATIVES OF SECONDARY AMINES

- Me₂NPSCl₂.** V. Liquid, *b*₁₆ 85–90°. ⁷⁷
Et₂NPSF₂. XX. Liquid, *b*₁₂ 50–1°. ⁴⁹
Et₂NPSCl₂. IV. XI. Liquid, *b*₁₄ 107°, *b*₁₃ 103°, *d*₀¹⁵ 1.105. ^{49, 77}
Et₂NPSBr₂. IV. Undistillable oil. ⁷⁷
Pr₂NPSCl₂. IV. V. Liquid, *b.* 240–5°, *b*₁₅ 132–4°, *d*₀¹⁵ 1.077. ⁷⁷
Pr₂NPSBr₂. IV. Undistillable oil. ⁷⁷
iso-Bu₂NPSCl₂. IV. V. XI. Crystals, *m.* 36° (from AcOH), *b*₁₀ 150°. ⁷⁷
iso-Bu₂NPSBr₂. IV. Plates, *m.* 66° (from Et₂O). ⁷⁷
iso-Am₂NPSCl₂. IV. V. Liquid, *b*₁₀ 160–63°, *d*₀¹⁵ 1.0288. ^{77, 84}
iso-Am₂NPSBr₂. IV. Undistillable oil. ⁷⁷
MePhNPSCl₂. IV. XI. Liquid, *d*₀²² 1.357. ⁷⁷
EtPhNPSCl₂. IV. XI. Undistillable liquid. ⁷⁷
C₆H₁₀NPSCl₂. IV. V. Liquid, *b*₂₁ 146–9°, *d*₀¹⁵ 1.3092. ⁷⁷

B. MONOHALOTHIONOPHOSPHATES

- (MeNH)₂PSF.** Liquid, *b*₂ 105°. ¹⁹
(Me₂N)(MeNH)PSF. Liquid, *b*₆ 93°. ¹⁹
(Me₂N)₂PSF. Liquid, *b*_{1,5} 58°. ¹⁹
(C₆H₁₀N)₂PSCl. IV. Plates, *m.* 98° (from Et₂O). ⁷⁷
(PhNH)(PhO)PSCl. X. Crystals, *m.* 153° (from EtOH). ¹²

304 COMPOUNDS WITH PHOSPHORUS TO NITROGEN BONDS

B. AMIDOPHOSPHITES

1. MONOAMIDOPHOSPHITES

iso-Bu₂NP(OPh)₂. I. Undistillable oil.⁷⁷

2. DIAMIDOPHOSPHITES

(Et₂N)₂POEt. I. Liquid, b₂₈ 105–8°.⁷⁷

(Pr₂N)₂POEt. I. Liquid, b₂₉ 143–7°.⁷⁷

(C₆H₁₀N)₂POEt. I. Liquid, b₂₇ 152–4°.⁷⁷

(iso-Bu₂N)₂POPh. I. Undistillable oil. On being heated with methyl iodide to 100°, it yields MeP(NBu-iso₂)₂I₂, m. 132°.⁷⁷

3. TRIAMIDES

(iso-BuNH)₃P. I. Undistillable liquid.⁷⁷

(C₁₂H₂₅NH)₃P. I. Colorless solid (from EtOH).⁸⁵

(PhCH₂NH)₃P. I. Undistillable oil.⁷⁷

(Et₂N)₃P. I. Liquid, b. 245–6°, b₁₀ 80–90°.⁷⁷

(Pr₂N)₃P. I. Liquid, b. 310–5°, b₁₅ 160–5°; methiodide, m. 83–4°.⁷⁷

(iso-Pr₂N)₃P. I. Liquid, b₁₈ 190–200°; methiodide, m. 138°.⁷⁷

(iso-Bu₂N)(C₆H₁₀N)₂P. I. Undistillable liquid.⁷⁷

(C₆H₁₀N)₃P. I. Crystals, m. 37–8°.⁸³

(C₉H₁₀N)₃P. I (from tetrahydroquinoline). Plates, m. 202–4° (from benzene).^{75, 77}

Tri-N,N',N''-(4-pyridyl)phosphorous amide. I (by-product). Crystals, m. 305–8°.⁸⁷

Tri-N-indolyl phosphorus. By-product from the reaction of PCl₃ with indole-magnesium. Crystals, m. 223–5° (from MeOH). Separated from the tri-3-indolylphosphine by insolubility in acetone. Readily decomposed by aqueous alkali.⁸⁶

Tri-N-(2-methylindolyl) phosphorus. Prepared as above from 2-methyl analog. Crystals, m. 180° (from MeOH).⁸⁶

4. SPECIAL CASE

(PhNHNH)₂POH. I, followed by water treatment. Powder, dec. 80°.⁸⁶ Appears to be a sole instance of free amidophosphite.

C. AMIDES OF PHOSPHONOUS ACIDS

PhP(NC₆H₁₀)₂. I. Plates, m. 78° (from Et₂O). Adduct with two molecules of carbon bisulfide, m. 144°, loses one molecule on crystallization and m. 137°.^{75, 77, 88}

PhP(NC₉H₁₀)₂. I (from tetrahydroquinoline). Crystals, m. 150°.^{75, 77}

4-ClC₆H₄P(NC₆H₁₀)₂. I. Crystals, m. 95°.⁸⁷

4-MeOC₆H₄P(NC₆H₁₀)₂. I. Crystals, m. 69°.⁸⁷

4-EtOC₆H₄P(NC₆H₁₀)₂. I. Crystals, m. 84°.⁸⁷

4-MeC₆H₄P(NC₆H₁₀)₂. I. Crystals, m. 80° (from Et₂O). Adduct with two molecules of carbon bisulfide, m. 139° (from benzene).^{75, 77, 80}

4-MeC₆H₄P(NC₉H₁₀)₂. I. Needles, m. 140°.^{75, 77}

D. AMIDES OF PHOSPHINOUS ACIDS

Ph(4-MeC₆H₄)PNHPh. I. Crystals, m. 124° (from EtOH).⁷⁶

Ph(4-MeC₆H₄)PNHC₆H₄Me-4. I. Needles, m. 142°.⁷⁶

E. AMIDOPHOSPHATES AND AMIDOTHIONOPHOSPHATES

1. MONOAMIDO DERIVATIVES

A. FREE ACIDS

Guanidine phosphate. XXIV (in 17 N NaOH). Calcium salt, crystals (from water or dil. EtOH).¹⁴⁰

Creatine phosphate. XXIV (in 17 N NaOH). Calcium salt (tetrahydrate), crystals (from dil. EtOH: in the presence of CaCl_2).¹³⁹

$\text{HO}_2\text{C}\cdot\text{CH}_2\text{NHPO}(\text{OH})_2$. XXIV (in presence of MgO). Magnesium salt.¹³⁷

$\text{HO}_2\text{C}\cdot\text{CMeH}\cdot\text{NHPO}(\text{OH})_2$. XXIV.¹³⁷ XXV.⁷ Magnesium salt.¹³⁷

$\text{HO}_2\text{C}(\text{CH}_2)_2\text{CH}(\text{CO}_2\text{H})\cdot\text{NHPO}(\text{OH})_2$. XXIV.¹³⁷ XXV.⁷ Magnesium salt.¹³⁷

Phosphoglycocycamine. XXIV. Calcium salt (trihydrate), crystals (from dil. EtOH in the presence of CaCl_2).³⁴

(O,N,N)-Tri-phospho-tyrosine. II (in pyridine, using tyrosine ethyl ester). Barium salt, crystals (from dil. EtOH).¹⁰⁸

$4\text{-ClC}_6\text{H}_4\text{NHPO}(\text{OH})_2$. XXIII. Needles, m. 155° (from dil. EtOH).^{77,101}

$4\text{-BrC}_6\text{H}_4\text{NHPO}(\text{OH})_2$. XXIII. Crystals, m. 158° .⁷⁷

$2,4\text{-Cl}_2\text{C}_6\text{H}_3\text{NHPO}(\text{OH})_2$. XXIII. Plates, m. 167° (from dil. EtOH).⁷⁷

$2\text{-Br-4-MeC}_6\text{H}_3\text{NHPO}(\text{OH})_2$. XXIII. Prisms, m. 142° (from dil. EtOH).⁷⁷

$\text{Ph}_2\text{NPO}(\text{OH})_2$. XXIII. Unstable crystals.¹⁰¹

$\text{PhCO}\cdot\text{NHPO}(\text{OH})_2$. XXIII. Crystals, m. $157\text{--}8^\circ$ (from benzene-MeOH).¹³⁰

B. PARTLY ESTERIFIED ACIDS

(EtO)(HO)PO \cdot NH \cdot PO(OH)(OEt) \cdot (?). Claimed to be the substance obtained by treatment of ethyl metaphosphate with ammonia in chloroform. Isolated as diammonium salt (from EtOH-Et₂O).⁶¹

(PhO)PO(OH)NH₂. By hydrolysis of the diphenyl ester with barium hydroxide solution. Barium salt, scales (from water). Cinchonine salt, needles, m. 194° (from water).^{31,125} Hydrolysis of the diphenyl ester by ammonium hydroxide yields an unstable ammonium salt. Silver salt, plates (from water).¹²⁵

(PhO)PNH₂(OSH). XXIII (using ammonium hydroxide).¹⁴ By hydrolysis of the diphenyl ester by alcoholic NaOH.³¹ Needles, m. $127\text{--}8^\circ$.¹⁴ Sodium salt (dihydrate), scales (from water).³¹

(PhO)PO(OH)NHNH₂. By hydrolysis of the diphenyl ester with aqueous sodium or ammonium hydroxide or with 10% barium hydroxide. Barium salt, plates (from water). Ammonium salt, crystals (from water). Sodium salt, needles (from EtOH).³³

(MeO)(PhNH)PO(OH). XXIII. Barium salt (heptahydrate), needles.²⁶

(EtO)(PhNH)PO(OH). XXIII. Barium salt, needles (from EtOH).²⁶

(PhO)(PhNH)PO(OH). XXIII. Plates, m. 134° (from EtOH-Et₂O). Silver salt, solid.⁷⁷

(PhO)(4-BrC₆H₄NH)PO(OH). XXIII. Crystals, m. 164° .⁷⁷

(4-MeC₆H₄O)(4-BrC₆H₄NH)PO(OH). XXIII. Plates, m. 230° .⁷⁷

(4-MeC₆H₄NH)(MeO)PO(OH). XXIII. Free acid is unstable. Potassium salt, needles. Barium salt (heptahydrate), needles (from water).²⁶

(4-MeC₆H₄NH)(EtO)PO(OH). XXIII. Barium salt, needles (from dil. EtOH).²⁶

Cholesteryl N,N-diphenyl-amidophosphate. RO \cdot PO(OH)NPh₂. X (in warm pyridine). Needles, m. 173° (from Me₂CO).¹⁴¹

C. DIESTER DERIVATIVES

i. DERIVATIVES OF AMMONIA AND HYDRAZINE

- (EtO)₂PONH₂. II.^{111,118} XXVI.¹⁰³ XXVII.⁵ Needles, m. 146°(?),¹⁰³ m. 54.5°, b_{0.2} 131–8°.¹¹¹ m. 53°.¹¹⁸ m. 50–1° (from cyclohexane-CCl₄).⁵
- (ClCH₂CH₂O)₂PONH₂. II. Crystals, m. 75–6°.¹¹⁸
- (iso-PrO)₂PONH₂. XXVII. Needles, m. 56–7° (from CHCl₃-ligroin).⁵
- (PhCH₂O)₂PONH₂. II.⁴ XXVII.⁵ Needles, m. 103.5–4.5° (from CCl₄).
- (PhO)(EtO)PONH₂. II. Crystals, m. 133°.⁹⁸
- (PhO)₂PONH₂. II.^{8, 31, 125} XXVII.⁶ Needles (from CHCl₃), m. 149–50°.⁶ m. 145–6°.⁸ dec. 180°.¹²⁵ m. 148°.^{31, 125}
- (PhO)₂PSNH₂. IV. Plates, m. 115° (from dil. EtOH),^{14, 31} m. 112°.³¹
- (PhO)₂PSeNH₂. IV. Crystals, m. 78° (from CCl₄).¹²⁷
- (4-ClC₆H₄O)₂PONH₂. II. Plates, m. 152° (from EtOH).¹¹
- (4-ClC₆H₄O)₂PSNH₂. II. Plates, m. 96° (from EtOH).¹⁴
- (4-MeC₆H₄O)₂PONH₂. II. Plates, m. 146° (from dil. EtOH).¹¹
- (4-MeC₆H₄O)₂PSNH₂. IV. Plates, m. 131° (from dil. EtOH).¹⁴
- (PhO)(2-C₁₀H₇O)PONH₂. II. Plates, m. 152–3° (from EtOH).⁵⁶
- (2-C₁₀H₇O)₂PONH₂. II. Plates, m. 215° (from EtOH).¹¹
- (2-C₁₀H₇O)₂PSNH₂. IV. Needles, m. 215° (from dil. EtOH).¹⁴
- (Ph₂CHO)₂PONH₂. XXVII. Needles, m. 145° (from cyclohexane).³
- (PhO)₂PO·NHNH₂. II. Crystals, m. 112° (from dil. EtOH).³³
- (PhO)₂PS·NHNH₂. IV.^{16, 127} Prisms, m. 63° (from ligroin),¹⁵ m. 62–3°.¹²⁷ Benzaldehyde forms a benzyldene derivative, m. 129°.¹⁶
- (PhO)₂PSe·NHNH₂. IV. Needles, m. 68° (from ligroin).¹²⁷
- (2-MeC₆H₄O)₂PSe·NHNH₂. IV. Crystals, m. 98–9° (from EtOH-benzene).¹²⁷
- (4-MeC₆H₄O)₂PS·NHNH₂. IV. Crystals, m. 141° (from EtOH).¹²⁷
- (4-MeC₆H₄O)₂PSe·NHNH₂. IV. Needles, m. 106–8°.¹²⁷
- (PhO)₂PO·NHNHPO(OPh)₂. By heating (PhO)₂PONHNH₂ above its melting point. Needles (from EtOH).³³

ii. DERIVATIVES OF PRIMARY AMINES

- (MeNH)PO(OEt)₂. II. Liquid, b₁₇ 135°.⁷⁰ b₁₅ 130°.¹¹¹
- (MeNH)PO(OPh)₂. II. Crystals, m. 95° (from ligroin).⁹
- (EtNH)PO(OEt)₂. X. Liquid, b₂₅ 135°.⁷⁸
- (EtNH)PO(OPh)₂. X. Liquid, b₁₁ 205°.⁷⁸
- (EtNH)PS(OEt)₂. X. Liquid, b₁₂ 94°.⁷⁷
- (EtNH)PS(OPh)₂. X. Liquid.⁷⁷
- (PrNH)PO(OEt)₂. X. Liquid, b₈ 112°.⁷⁸
- (PrNH)PO(OPh)₂. X. Liquid, b₈ 208°.⁷⁸
- (PrNH)PS(OEt)₂. X. Liquid, b₁₁ 98°, d₀¹⁵ 1.005.⁷⁷
- (iso-BuNH)PO(OEt)₂. X. Liquid, b₁₄ 146°.⁷⁸
- (iso-BuNH)PO(OPh)₂. X. Needles, m. 58°, b₁₁ 218°.⁷⁸
- (iso-BuNH)PO(OEt)₂. X. Liquid, b₁₂ 104°.⁷⁷
- (iso-AmNH)PO(OEt)₂. X. Liquid, b₂₅ 185°.⁷⁸
- (C₁₂H₂₅NH)PO(OEt)₂. X. Liquid, b₆ 180–90°.⁸⁵
- (H₂NC(:NH)NH)PO(OPh)₂. II. Crystals, m. 118°.¹¹⁴
- (H₂NC(:NH)NH)PO(OCH₂Ph)₂. II. Crystals, m. 166.5–7.5°.³⁰
- (Cl₂CH·CONH)PO(OEt)₂. X. Needles, m. 72–3° (from water).^{123, 124}
- (ClBrCH·CONH)PO(OEt)₂. X. Crystals, m. 67–8° (from water).¹²³
- (MeOCBr₂·CONH)PO(OMe)₂. X (from the tribromoacetyl derivative). Crystals, m. 92–3° (from water).^{123, 124}

(EtOCBr₂·CONH)PO(OEt)₂. X (from the tribromoacetyl derivative). Needles, m. 91° (from water).¹²³

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(Cl₃CCNH)PO(OMe)₂. X. Plates, m. 105–7° (from water).^{123, 124}

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(Cl₃CCNH)PO(OEt)₂. X. Crystals, m. 47–8° (from ligroin).^{123, 124}
(Cl₂BrC·CONH)PO(OMe)₂. X. Crystals, m. 107° (from water).^{123, 124}
(Cl₂BrC·CONH)PO(OEt)₂. X. Crystals, m. 76–7° (from water).^{123, 124}
(O₂N·CCl₂·CONH)PO(OEt)₂. X. Needles, m. 56° (from ligroin).^{123, 124}
(Ph₂CCl·CONH)PO(OMe)₂. X. Crystals, m. 104–6°.^{123, 124}
(EtO₂C·CH₂NH)PO(OPh)₂. II. Crystals, m. 76°.¹¹⁴

(PhCH₂NH)PO(OPh)₂. II. Crystals, m. 104–5° (from benzene).⁷⁷

(PhCH₂NH)PO(OCH₂Ph)₂. II. Needles, m. 84–5° (from benzene-ligroin).⁴

(PhCH₂NH)PO(OCHPh)₂. XXVII. Needles, m. 104–5° (from cyclohexane-ligroin).⁸

(MePhCHNH)PO(OCH₂Ph)₂. II. Needles, m. 81–2° (from ligroin).⁴

(PhNH)PO(OMe)₂. II. Crystals, m. 88–8.5°.⁷⁰

(PhNH)PO(OEt)₂. II.^{3, 69, 70} X.⁹¹ Plates (from benzene or Et₂O), m. 96.5°;⁶⁹ m. 95.5–6.5°;⁷⁰ m. 95–6°;³ m. 93°.⁹¹

(PhNH)PO(OPr-iso)₂. II.^{3, 69, 70} Crystals, m. 121–1.5°;^{69, 70} m. 120–1°.³

(PhNH)PO(OCH(CH₂Cl)₂)₂. II. Crystals, m. 81° (from dil. AcOH).²⁸

(PhNH)PO(Obu-iso)₂. II. Crystals, m. 43.5–45°.²⁸

(PhNH)PO(OCHMe·CO₂Et)₂. II. Crystals, m. 91° (from dil. EtOH).²⁸

(PhNH)PO(OCH₂Ph)₂. II.^{3, 4} XXVII (using dimethylcyclohexylamine as catalyst).⁵ Plates, m. 91–2.5° (from dil. EtOH),^{4, 5} m. 91–2° (from cyclohexane).³

(PhNH)PO(OEt)(OPh). II.⁹⁸ X (using (PhO)(PhNH)POCl).⁷⁷ Needles, m. 143°;⁹⁸ m. 120°.⁷⁷

(PhNH)PO(OPh)₂. II.⁹ IX (using a mixture of aniline and phenol),¹³⁸ (using (PhO)₃PCl₂).¹³ X.⁹¹ Plates, m. 129–30° (from EtOH),⁹ m. 129°;⁹¹ m. 127–9° (from EtOH).¹³³

(PhNH)PS(OPh)₂. IV (using 10% NaOH). Prisms, m. 92° (from EtOH).¹⁴

(PhNH)PO(OC₆H₄Me-2)₂. IX (using (RO)₃PCl₂). Prisms, m. 126–7°.¹⁸

(PhNH)PO(OC₆H₄Me-3)₂. IX (using (RO)₃PCl₂). Prisms, m. 82° (from dil. EtOH).¹³

(PhNH)PO(OPh)(OC₆H₄Me-4). X. Crystals, m. 106° (from dil. EtOH).⁷⁷

(PhNH)PO(OC₆H₄Me-4)₂. IX (using (RO)₃PCl₂).¹³ X.⁹¹ Crystals, m. 133°;⁹¹ m. 125° (from EtOH).¹³

(PhNH)PS(OC₆H₄Me-4)₂. IV (using dil. NaOH). Needles, m. 106°.¹⁴

(PhNH)PO(OC₁₀H₇-2)₂. IX (using (RO)₃PCl₂). Needles, m. 193–5°.¹⁸

Dicholesteryl N-phenyl-amidophosphate. (RO)₂PO(NHPh). X (using pyridine). Crystals, m. 196–7° (from PhNO₂).¹⁴²

(Ethyl N-phenyl-amidophosphoryl)-1,2,3,4-tetra-acetyl-glucose. X (using pyridine). Crystals, m. 116–7° (from benzene-ligroin).¹⁴¹

(4-ClC₆H₄NH)PO(OEt)₂. X.¹⁰¹ Plates, m. 76°.¹⁰¹

(4-ClC₆H₄NH)PO(OPh)₂. X. Plates, m. 117° (from EtOH).¹⁰¹

(3-BrC₆H₄NH)PO(OC₁₀H₇-2)₂. X. Needles, m. 166.5°.⁷⁷

(4-BrC₆H₄NH)PO(OPh)₂. X. Plates, m. 112° (from EtOH).⁷⁷

(4-BrC₆H₄NH)PO(OC₆H₄Me-4)₂. X. Needles, m. 138°.⁷⁷

(2,4-Cl₂C₆H₃NH)PO(OEt)₂. X. Needles, m. 106° (from Et₂O).⁷⁷

(2,4-Cl₂C₆H₃NH)PO(OPh)₂. X. Crystals, m. 132° (from Et₂O).⁷⁷

- (2,4-Cl₂C₆H₃NH)PO(OC₆H₄Me-4)₂.** X. Crystals, m. 162°. ⁷⁷
(2,4-Br₂C₆H₃NH)PO(OEt)₂. X. Plates, m. 114°. ⁷⁷
(2,4-Br₂C₆H₃NH)PO(OPh)₂. X. Needles, m. 141° (from EtOH). ⁷⁷
(2,4-Br₂C₆H₃NH)PO(OC₆H₄Me-4)₂. X. Crystals, m. 158°. ⁷⁷
(3-O₂NC₆H₄NH)PO(OEt)₂. X. Crystals, m. 120°. ⁷⁷
(2-MeC₆H₄NH)PO(OEt)₂. X. Plates, m. 95°. ⁹¹
(2-MeC₆H₄NH)PO(OPh)₂. X. Plates, m. 176° (from EtOH). ⁹¹
(2-MeC₆H₄NH)PO(OC₆H₄Me-2)₂. X. Scales, m. 161°. ⁹¹
(4-MeC₆H₄NH)PO(OEt)₂. X. Crystals, m. 98°. ⁹¹
(4-MeC₆H₄NH)PO(OPh)₂. X. Plates, m. 134° (from EtOH). ⁹¹
(4-MeC₆H₄NH)PO(OCH₂Ph)₂. XXVII. Crystals, m. 89.5–90.5° (from hexane). ⁶
(4-MeC₆H₄NH)PO(OC₆H₄Me-4)₂. X. Needles, m. 161°. ⁹¹
(4-MeC₆H₄NH)PO(OPh)(OC₁₀H₇-2). II. Crystals, m. 126–7°. ⁵⁵
(2-Br-4-MeC₆H₃NH)PO(OEt)₂. X. Needles, m. 102°. ⁷⁷
(2-Br-4-MeC₆H₃NH)PO(OPh)₂. X. Needles, m. 126° (from EtOH). ⁷⁷
(2-Br-4-MeC₆H₃NH)PO(OC₆H₄Me-4)₂. X. Crystals, m. 154°. ⁷⁷
(2-PhO₂C·C₆H₄NH)PO(OPh)₂. X (using the 2-chloroformyl derivative). Crystals, m. 94° (from EtOH). ¹³¹
(3-MeO₂C·C₆H₄NH)PO(OMe)₂. X (as above). Liquid, b. 184–6°(?). ⁷⁷
(3-EtO₂C·C₆H₄NH)PO(OEt)₂. X (as above). Liquid, b. 232–4°, b₃₅ 130–5°. ⁷⁷
(4-MeO₂C·C₆H₄NH)PO(OMe)₂. X (as above). Liquid, b. 166–7°(?). ⁷⁷
(4-EtO₂C·C₆H₄NH)PO(OEt)₂. X (as above). Liquid, b. 206–7°, b_{45–50} 113–8°. ⁷⁷
(2,4-Me₂C₆H₃NH)PO(OEt)₂. X. Crystals, m. 96°. ⁷⁷
(2,4-Me₂C₆H₃NH)PO(OPh)₂. X. Crystals, m. 115°. ⁷⁷
(2-C₁₀H₇NH)PO(OCH₂Ph)₂. XXVII. Crystals, m. 75.5–6.5°. ⁶
(C₆H₁₁NH)PO(OCH₂Ph)₂. II. ⁴ XXVII. ⁶ Needles, m. 79–80° (from ligroin).
(C₆H₁₁NH)PO(OPh)₂. II. Crystals, m. 104–5° (from dil. EtOH). ⁹
(C₆H₁₁NH)PO(OCHPh)₂. XXVII. Needles, m. 101–2° (from cyclohexane). ³
Phenyl *p*-tolyl N-menthyl-amidophosphate. II (from levo form of the amine).
 Two forms: m. 109–10° and m. 85–6° (from dil. EtOH); the low-melting form is more soluble in organic solvents. ⁶⁷
Phenyl 2-naphthyl N-menthyl-amidophosphate. II (from levo form of the amine). Two forms: m. 135–6° (from dil. Me₂CO) and m. 94–6° (from MeOH). ⁵⁵
Phenyl *p*-tolyl N-(levo)-hydrindyl-amidophosphate. II. Inactive form: (from *dl*-amine), prisms, m. 98–100° (from MeOH). Active form: two isomers (apparently), m. 127° and m. 82–6° (from dil. MeOH), obtained from *d*-amine. ⁶⁷
(PhNHNH)PO(OEt)₂. II. Crystals, m. 113–4°. ⁷³
(PhNHNH)PS(OEt)₂. IV. Crystals, m. 68–9°. ⁷³
(PhNHNH)PO(SET)₂. IV. Crystals, m. 106.5–7.0°. ⁷³

iii. DERIVATIVES OF SECONDARY AMINES

- (Me₂N)PO(OMe)₂.** X. Liquid, b₁₅ 80°. ¹²²
(Me₂N)PS(OMe)₂. X. Liquid, b₁₅ 90°. ¹²²
(Me₂N)PO(OEt)₂. X. Liquid, b₁₃ 92°. ¹²² b₅ 85–90°. ⁷⁷
(Me₂N)PS(OEt)₂. X. Liquid, b₄₅ 107°. ⁷⁷
(Me₂N)PO(OCH₂CH₂OMe)₂. X. Liquid, b₁₃ 155–6°. ¹²²
(Me₂N)PO(OEt)(OPh). Liquid, b₁ 156°. ¹⁹
(Me₂N)PO(OEt)(OC₆H₄NO₂-2). Liquid, b₁ 156°(?). ¹⁹
(Me₂N)PO(OEt)(OC₆H₄NO₂-4). Liquid, b₂ 185°. ¹⁹
(Me₂N)PO(OEt)(OC₆H₄CO₂Et-2). Liquid, b₂ 160°. ¹⁹
(Et₂N)PO(OMe)₂. X. Liquid, b₂₂ 100°. ¹²²

- $(\text{Et}_2\text{N})\text{PO}(\text{OEt})_2$. X. Liquid, b. $218-20^\circ$,⁷⁷ b_{25} $114-7^\circ$,⁷⁷ b_{18} 109° .¹³²
 $(\text{Et}_2\text{N})\text{PS}(\text{OEt})_2$. X. Liquid, b_{20} 110° , d_0^{15} 1.0056.⁷⁷
 $(\text{Et}_2\text{N})\text{PO}(\text{OCH}_2)_2$. X. Undistillable oil.¹³²
 $(\text{Et}_2\text{N})\text{PO}(\text{OCH}_2\text{CH}_2\text{OH})$. X. Undistillable oil.¹³²
 $(\text{Et}_2\text{N})\text{PO}(\text{OCH}_2\text{CH}_2\text{OMe})_2$. X. Liquid, b_{13} 165° .¹³²
 $(\text{Et}_2\text{N})\text{PO}(\text{OCH}_2\text{CH}_2\text{OEt})_2$. X. Liquid, b_{10} $167-70^\circ$.³⁰
 $(\text{Et}_2\text{N})\text{PO}(\text{OPh})_2$. X. Undistillable oil.⁷⁷
 $(\text{Et}_2\text{N})\text{PS}(\text{OPh})_2$. II.¹⁴ X.⁷⁷ Prisms, m. 70° (from EtOH),⁷⁷ m. 58° .¹⁴
 $(\text{Et}_2\text{N})\text{PO}(\text{OEt})\text{CN}$. X-XX (using KCN-EtOH). Crude liquid only obtained by Michaelis.⁷⁷ Liquid, b_{17} 124° .¹³²
 $(\text{Et}_2\text{N})\text{PO}(\text{SCN})_2$. XX (using NH_4SCN). Crystals, m. 151° (from EtOAc).¹³²
 In very crude state: XX (using AgSCN).⁷⁷
 $(\text{Et}_2\text{N})\text{PO}(\text{:NCN})$. XX (using sodium cyanamide). Undistillable oil.¹³²
 $(\text{Pr}_2\text{N})\text{PO}(\text{OEt})_2$. X. Liquid, b_{12} $105-10^\circ$, d_0^{15} 0.975.⁷⁷
 $(\text{Bu}_2\text{N})\text{PO}(\text{OCH}_2\text{CH}_2\text{OMe})_2$. X. Liquid, b_6 $172-8^\circ$.¹¹⁸
 $(\text{Bu}_2\text{N})\text{PO}(\text{OCH}_2\text{CH}_2\text{OBu})_2$. X. Liquid, b_4 $198-205^\circ$.¹¹⁸
 $(\text{Bu}_2\text{N})\text{PO}(\text{OBu})_2$. II. Liquid, b_6 $158-61^\circ$.¹¹⁸
 $(\text{iso-Bu}_2\text{N})\text{PO}(\text{OEt})_2$. X. Liquid, d_0^{14} 0.9663.⁷⁷
 $(\text{iso-Bu}_2\text{N})\text{PO}(\text{OPh})_2$. X. Crystals, m. 56° .⁷⁷
 $(\text{iso-Am}_2\text{N})\text{PS}(\text{OMe})_2$. X. Liquid, b_{13} $118-21^\circ$, d_0^{15} 1.0024.⁷⁷
 $(\text{iso-Am}_2\text{N})\text{PS}(\text{OPh})_2$. X. Needles, m. 64° .⁷⁷
 $(\text{MePhN})\text{PO}(\text{OEt})_2$. X. Undistillable liquid.⁷⁷
 $(\text{MePhN})\text{PO}(\text{OPh})_2$. X. Needles, m. 50° .⁷⁷
 $(\text{MePhN})\text{PO}(\text{OCH}_2\text{Ph})_2$. XXVII (using CBrCl_3). Crystals, m. $86-7^\circ$.⁶
 $(\text{EtPhN})\text{PS}(\text{OEt})_2$. X. Undistillable liquid.⁷⁷
 $(\text{Ph}_2\text{N})\text{PO}(\text{OEt})_2$. X. Plates, m. 175° .¹⁰¹
 $(\text{Ph}_2\text{N})\text{PO}(\text{OPh})_2$. X. Needles, m. 180° (from EtOH).¹⁰¹
 $(\text{Ph}_2\text{N})\text{PO}(\text{OC}_6\text{H}_4\text{Me-2})_2$. X. Plates, m. 178° (from EtOH).¹⁰¹
 $(\text{C}_6\text{H}_{10}\text{N})\text{PO}(\text{OMe})_2$. X. Liquid, b_{13} 125° .¹³²
 $(\text{C}_6\text{H}_{10}\text{N})\text{PO}(\text{OEt})_2$. II. Liquid.⁷⁷
 $(\text{C}_6\text{H}_{10}\text{N})\text{PS}(\text{OEt})_2$. X. Liquid, b_{10} 138° , d_0^{16} 1.0433.⁷⁷
 $(\text{C}_6\text{H}_{10}\text{N})\text{PO}(\text{OCH}_2\text{CH}_2\text{OEt})_2$. X (using ROK). Liquid, b_{22} $210-3^\circ$.³⁰
 $(\text{C}_6\text{H}_{10}\text{N})\text{PO}(\text{OPh})_2$. II. Prisms, m. 70° .⁷⁷
 $(\text{C}_6\text{H}_{10}\text{N})\text{PS}(\text{OPh})_2$. X. Liquid.⁷⁷
 $(\text{O}(\text{CH}_2\text{CH}_2)_2\text{N})\text{PO}(\text{OEt})_2$. II. Liquid, b_{11} 137° .¹¹¹
 $(\text{O}(\text{CH}_2\text{CH}_2)_2\text{N})\text{PO}(\text{OPh})_2$. II. Crystals, m. $72.5-3.5^\circ$ (from ligroin), b_5 $240-50^\circ$.⁹
 $(\text{O}(\text{CH}_2\text{CH}_2)_2\text{N})\text{PO}(\text{OCH}_2\text{Ph})_2$. XXVII. Prisms, m. $71-2^\circ$ (from cyclohexane).⁵
 $(\text{C}_9\text{H}_{10}\text{N})\text{PO}(\text{OEt})_2$. II (from tetrahydroquinoline). Liquid, b_8 155° .⁷⁷
 $(\text{C}_9\text{H}_{10}\text{N})\text{PO}(\text{OPh})_2$. II. Liquid.⁷⁷

2. DIAMIDO DERIVATIVES

A. FREE ACIDS

i. DERIVATIVES WITH FREE AMIDO GROUPS

The correct formulation of these substances is not certain. They may be the acid ammonium salts of the N-substituted monoamides.

- $(\text{Et}_2\text{N})\text{PO}(\text{NH}_2)\text{OH}$. XIXA. Needles, m. 144° .⁷⁷
 $(\text{PhNH})\text{PO}(\text{NH}_2)\text{OH}$. II-XXIII. Plates, m. $157-8^\circ$.³⁶
 $(4\text{-MeC}_6\text{H}_4\text{NH})\text{PO}(\text{NH}_2)\text{OH}$. II-XXIII. Plates, m. 159° .³⁶

310 COMPOUNDS WITH PHOSPHORUS TO NITROGEN BONDS

- 4-H₂N·SO₂·C₆H₄NHPO(NH₂)OH.** II-XXIII. III-XXIII. Crystals, m. 167-9°; unstable in hot water. Sodium salt is stable.^{47,135}
4-H₂N·SO₂·C₆H₄NMePO(NH₂)OH. II-XXIII. Solid.⁴⁸

ii. DERIVATIVES WITH SUBSTITUTED AMIDO GROUPS

- O:C(NH)₂PS(SH).** XVIII.^{45,58} Free acid (dihydrate), dec. 78°. Ammonium salt, plates, dec. 252° (from water).⁵⁸ Barium salt, plates.⁴⁵ Silver salt, solid, unstable to light.⁴⁵
(PhNH)₂PO(OH). XXIII.^{91,93} XXIV.¹⁶ XXVIII.²⁵ Plates, m. 214-6°;¹⁶ m. 213°;^{77,91,93} m. 199-200°.²⁵ Copper salt, plates, somewhat soluble in hot water. Silver salt, colorless solid.
(PhNH)₂PS(SH). XVIII. Crystals, m. 161-3°; very poorly stable. Metal salts are insoluble.²³
(2-ClC₆H₄NH)₂PS(SH). XVIII. Crystals, m. 183-90°.²³
(4-ClC₆H₄NH)₂PO(OH). XXIV. Crystals, dec. 218°.¹⁶ XXIII. Plates, m. 126° (from water).¹⁰¹ This preparation is one of the most controversial in the field of phosphorus chemistry.
(4-EtOC₆H₄NH)₂PO(OH). XXIV. Crystals, m. 202° (from EtOH-Et₂O).¹⁶ Sodium salt, needles (from EtOH-Et₂O), prisms (from Me₂CO-Et₂O).¹⁶
(4-EtOC₆H₄NH)₂POSH. XXIV. Colorless solid. Unstable.¹⁶
(2-MeC₆H₄NH)₂PO(OH). XXIII. Crystals, m. 120°. Copper salt, insoluble. Barium salt, needles (from water).^{91,110}
(PhNH)(4-MeC₆H₄NH)PO(OH). XXIII. Plates, shrink at 134°, solidify and m. 195-6° (from Me₂CO-dil. HCl).²⁶
(4-MeC₆H₄NH)₂PO(OH). XXIII.^{91,110} XXIV.¹⁶ Crystals, soften at 148°, m. 193-4°;²⁶ m. 195°.¹⁶ Copper salt, needles (from water). Barium salt, needles (from water).
(C₉H₁₀N)(PhNH)PO(OH). XXIII. Unstable crystals.⁷⁷
p-(H₂NC₆H₄·SO₂·C₆H₄NH·PO₂H·NHC₆H₄·SO₂·C₆H₄NH)₂PO₂H. XXIII (from bis-dichlorophosphoryl derivative of diaminodiphenylsulfone). Free acid, amorphous solid. Sodium salt, amorphous. Derivative of *p*-dimethylaminobenzaldehyde, m. 218-9°. Hydrolysis of the above chloro derivative results in complex mixtures of polyphosphorylated products.⁵⁰
MePhNPO(NH₂)OH. II-XXIII. Plates, m. 125°.⁷⁷ (Although fairly well characterized, this compound may really belong in group i.)
(PhCONH·NPh)₂PO(OH). IX. Prisms, m. 131-2° (from MeOH).¹⁰²

B. ESTER DERIVATIVES

i. DERIVATIVES OF AMMONIA AND HYDRAZINE

- PhOPO(NH₂)₂.** II.^{3,136} Plates (from EtOH), dec. 185-90°;¹³⁶ m. 183-5°.³
PhOPS(NH₂)₂. IV.^{14,22} Plates (from water), m. 119°;¹⁴ m. 118°.²²
4-MeC₆H₄OPS(NH₂)₂. IV. Crystals, m. 84° (from EtOH).¹²⁸
4-*tert*-AmC₆H₄OPO(NH₂)₂. II. Crystals, m. 160°.⁹⁷
2-C₁₀H₇OPS(NH₂)₂. II. Plates, m. 176° (from EtOH-Me₂CO).¹⁴
2-PhC₆H₄OPO(NH₂)₂. II. Crystals, m. 151°.⁹⁷
EtOPO(NHPh)(NH₂). II. Prisms, m. 127° (from water).²⁶
EtOPO(NHC₆H₄Me-4)(NH₂). II. Plates, m. 125° (from EtOAc-ligroin).²⁶
PhOPO(NHNH₂)₂. II. Crystals, m. 100° (from dil. EtOH).¹²⁸
PhOPO(NHNH)₂PO(OPh). II (hydrazine added to the chlorophosphate). Plates, m. 132° (from EtOH).¹³

- PhOPS(NHNH₂)₂**. IV.^{15, 128} Plates, m. 95° (from EtOH).^{15, 128} Dibenzylidene derivative, m. 115° (from EtOH).¹⁵
- PhOPS(NHNH)₂PS(OPh)**. IV (using a deficiency of hydrazine, in glycerol solution). Prisms, m. 183° (from EtOH).¹⁵
- 4-MeC₆H₄OPS(NHNH₂)₂**. IV. Crystals, m. 106° (from EtOH).¹²⁸
- 4-MeC₆H₄OPO(NHNH)₂PO(OC₆H₄Me-4)**. II. Plates, m. 168° (from EtOH).¹²
- PhOPS(NHNHPh)₂**. IV. Needles, m. 136° (from EtOH).¹⁴
- 2-PhO₂C·C₆H₄OPO(NHNHPh)₂**. II. Needles, m. 170°. ⁸²
- 1-C₁₀H₇OPO(NHNHPh)₂**. II. Crystals, m. 168-9° (from EtOH).⁶⁰
- 2-C₁₀H₇OPO(NHNHPh)₂**. II. Crystals, m. 198° (from AcOH).⁶⁰

ii. DERIVATIVES OF PRIMARY AMINES

- (MeNH)₂PO(OPh)**. II. Crystals, m. 103-5° (from CCl₄).⁹
- (CH₂NH)₂PO(OPh)**. II (in aqueous solution). Powder, m. 196°. ¹²
- (CH₂NH)₂PS(OPh)**. IV. Poorly soluble powder, m. 189°. ¹⁵
- (CH₂NH)₂PO(OC₆H₄Me-4)**. II. Powder, m. 204°. ¹²
- (PrNH)₂PO(OEt)**. X. Needles, m. 108°. ⁷⁸
- (iso-BuNH)₂PO(OEt)**. X. Needles, m. 123°. ⁷⁸
- (PhNH)₂PO(OEt)**. II. X. Plates, m. 114° (from dil. EtOH). ⁷⁷
- (PhNH)₂PO(OPh)**. II.^{9, 77} X.^{77, 91, 92} XXIX.^{77, 92} Needles. The melting point varies even with apparently identical procedures: m. 179-80°, ⁹ m. 179.5°, ⁷⁷ m. 169°, ⁷⁷ m. 165°, ⁹² m. 126°, ¹⁵ m. 125°. ⁹¹ (from dil. EtOH).
- (PhNH)₂PS(OPh)**. IV (in 10% NaOH). Crystals, m. 126° (from EtOH).^{14, 15} Acidification of the alkaline solution after the removal of the above product yields a substance that has been assigned the ortho structure: (PhO)(PhNH)₂P(SH)-(OH).¹⁵ This material forms needles, m. 155° (from dil. EtOH), titrates as a monobasic acid, forming a sodium salt, needles (from EtOH). On heating, this substance slowly loses H₂S and forms (PhO)(PhNH)₂PO. The ortho compound, in the form of its sodium salt, reacts with iodine, forming a disulfide (probably of phosphatogen type), m. 165° (from MeOH or EtOH), assigned the structure ((PhO)(PhNH)P(O)S—)₂.
- (PhNH)₂PO(OC₆H₄Cl-4)**. II. X. Crystals, m. 167-8°. ⁷⁷
- (PhNH)₂PO(OC₆H₄CO₂Ph-2)**. II. Needles, m. 174-5° (from EtOH). ⁸²
- (PhNH)₂PO(OCH₂·CHOH·CH₂O₂C·C₆H₄NO₂-4)·(?)**. X. Crystals, m. 220°. ¹⁴²
- Cholesteryl N,N'-diphenyl-diamidophosphate**. RO·PO(NHPh)₂. X (in pyridine). Crystals, m. 182°. ¹⁴²
- Octa-(N,N'-diphenyl-diamidophosphoryl) sucrose**. X (in pyridine). Crystals, m. 219-20°. ¹⁴²
- o-C₆H₄(NH)₂PO(OPh)**. II. Crystals, m. 185° (from EtOH).¹²
- o-C₆H₄(NH)₂PS(OPh)**. IV. Prisms, m. 185° (from EtOH).¹⁴
- o-C₆H₄(NH)₂PO(OC₆H₄Me-4)**. II. Crystals, m. 158°. ¹²
- o-C₆H₄(NH)₂PS(OC₆H₄Me-4)**. IV. Prisms, m. 147° (from EtOH).¹⁵
- o-C₆H₄O₂(PO(NHPh)₂)₂**. X (in pyridine). Crystals, m. 192° (from EtOH).¹⁴²
- (2,4-Cl₂C₆H₃NH)₂PO(OPh)**. XXIX. Crystals, m. 227° (from EtOH). ⁹²
- (4-EtOC₆H₄NH)₂(PhO)P(SH)(OH)**. Structure assigned to the substance obtained by reaction II (using PhOPSCl₂ in 10% NaOH). Prisms, m. 145° (from EtOH). Reaction of its sodium salt with iodine yields a "disulfide," apparently a phosphatogen of structure ((PhO)(4-EtOC₆H₄NH)P(O)S—)₂, m. 153°. ¹⁵
- (PhCH₂NH)₂PO(OPh)**. II. Needles, m. 114°. ⁷⁷
- (PhCH₂NH)₂PS(OPh)**. IV. Needles, m. 73°. ⁷⁷
- (2-MeC₆H₄NH)₂PO(OEt)**. II. X. Needles, m. 115°. ⁷⁷

- (2-MeC₆H₄NH)₂PO(OPh). II. X. Scales, m. 157.5°. ⁷⁷
 (PhNH)(4-MeC₆H₄NH)PO(OEt). II. Needles, m. 116-7° (from dil. EtOH). ³⁶
 (PhNH)(4-MeC₆H₄NH)PO(OPh). II. Needles, m. 136-7°. ⁷⁷
 (4-MeC₆H₄NH)₂PO(OEt). II. Prisms, m. 108° (from dil. EtOH). ⁷⁷
 (4-MeC₆H₄NH)₂PO(OPh). II. Crystals, m. 147-8° (from dil. EtOH). ⁵⁵
 (4-MeC₆H₄NH)₂PO(OC₆H₄CO₂Ph-2). II. Needles, m. 146° (from EtOH). ⁸³
 (2-Br-4-MeC₆H₃NH)₂PO(OPh). XXIX. Plates, m. 221°. ⁹²
 (2-MeO₂C·C₆H₄NH)₂PO(OMe). X (from the chloroformyl derivative). Needles, m. 174° (from MeOH). ¹³¹
 (C₆H₁₁NH)₂PO(OPh). II. Crystals, m. 124-5° (from dil. EtOH). ⁹
 (PhNH)₂PO·OCH₂CH₂O·PO(NHPh)₂. X (in pyridine). Crystals, m. 180°. ¹⁴²
 1,2,3-Tri-(N,N'-diphenyl-diamidophosphoryl) glycerol. X. ¹⁴³ Crystals, m. 206°.

iii. DERIVATIVES OF SECONDARY AMINES

- (Me₂N)₂PO(OPh). Liquid, b_{0.5} 158-60°. ¹⁹
 (Me₂N)₂PO(OC₆H₄NH₂-4). Liquid, b. 136°(?). ¹⁹
 (Me₂N)₂PO(OC₆H₄NO₂-2). Liquid, b_{0.5} 166°. ¹⁹
 (Me₂N)₂PO(OC₆H₄NO₂-3). Liquid, b₁ 175°. ¹⁹
 (Me₂N)₂PO(OC₆H₄NO₂-4). Liquid, b₁ 192°. ¹⁹
 (Et₂N)₂PO(OEt). II. Liquid, b₁₅ 140°. ⁷⁷
 (Et₂N)₂PS(OEt). XI. Liquid, b₂₀ 149-51°. ⁷⁷
 (Et₂N)₂PO(OCH₂CH₂OEt). II. Liquid, b₁₅ 170-80°. ³⁰
 (Pr₂N)₂PO(OEt). XVI. Liquid, b₂₀ 164-6°. ⁷⁷
 (Pr₂N)₂PS(OEt). XI. Liquid, b₂₂ 178-80°. ⁷⁷
 (Et₂N)(C₆H₁₀N)PO(OEt). II. Liquid, b₁₅ 150°. ⁷⁷
 (C₆H₁₀N)₂PO(OEt). II. XVI. Liquid, b₂₀ 176-80°. ⁷⁷
 (C₆H₁₀N)₂PS(OEt). XI. Liquid, b₂₂ 198-210°, b₁₀ 191°, d₀¹⁵ 1.0633. ⁷⁷
 (C₆H₁₀N)₂PO(OPh). II. X. Liquid, b₁₀ 215-6°. ⁷⁷
 (C₆H₁₀N)₂PS(OPh). X. XI. Needles, m. 108°. ⁷⁷
 (O(CH₂CH₂)₂N)₂PO(OPh). II. Crystals, m. 85-6° (from ligroin), b₂ 220°. ⁹
 3,6-Di-(N,N-diphenylamidophosphoryl)-methylglucoside. X (in pyridine). Crystals, m. 251°. Diacetate, m. 138°. ¹⁴¹

3. TRIAMIDO DERIVATIVES

A. DERIVATIVES OF AAAP TYPE

i. DERIVATIVES OF PRIMARY AMINES

- (EtNH)₃PS. IV. Crystals, m. 68°. ⁷⁷
 (PrNH)₃PO. II. Oil. ⁷⁷
 (PrNH)₃PS. IV. ⁷⁷ XVIII. ²³ Needles, m. 73°. ⁷⁷
 (iso-BuNH)₃PO. II. Crystals, m. 46-7°. ⁷⁷
 (iso-BuNH)₃PS. IV. Crystals, m. 78-8.5°. ⁷⁷
 (iso-AmNH)₃PO. II. Undistillable liquid. ^{77, 78}
 (iso-AmNH)₃PS. IV. Undistillable liquid. ^{77, 78}
 (C₁₂H₂₅NH)₃PO. II. Crystals, m. 75° (from Et₂O). ²⁵
 (PhCH₂NH)₃PO. II. ⁷⁷ II (using pyridine). ¹⁰ XII. ⁷⁷ Needles (from EtOH), m. 98-9°, ¹⁰ m. 98°. ⁷⁷
 (PhCH₂NH)₃PS. IV. ⁷⁷ XVIII. ²³ XVIII. ²³ Needles, m. 127°, ⁷⁷ m. 125-6°. ²³
 (PhNH)₃PO. II ^{10, 21, 33, 100, 115} (the last-named reference: using pyridine). IX. ^{23, 54} XII. ⁵⁴ XXIV. ¹⁶ XXIX. ^{26, 78, 92} Needles or plates (from EtOH), m. 213-5°, ²⁵ m. 212-5°, ¹⁶ m. 211-4°, ¹⁰ m. 212°, ¹⁰⁰ m. 208-10°, ²³ m. 208°. ⁷⁸

- (PhNH)₃PS.** XVIII.^{23, 56, 110} XVIIIA.²³ XXIV.¹⁶ Crystals (from AcOH or EtOH), m. 153–4°, ^{16, 23} m. 153°. ⁵⁶
(4-ClC₆H₄NH)₃PO. III.¹⁰¹ XXIV.¹⁶ Plates or needles (from EtOH-H₂O), m. 248–50°, ¹⁶ m. 230°. ¹⁰¹
(4-ClC₆H₄NH)₃PS. XVIII. Crystals, m. 225–6°. ²³
(4-Cl-2(or 3)-O₂NC₆H₃NH)₃PO. By nitration of the above compound in acetic acid. Yellow needles, m. 249°. ¹⁰¹
(2,4(?) -Br₂C₆H₃NH)₃PO. By bromination of the triphenyl analog in acetic acid. Needles, m. 252–3° (from AcOH). ⁹³
(4-EtOC₆H₄NH)₃PO. II (using pyridine). ¹⁰ XXIV.¹⁶ Crystals (from dil. EtOH), m. 172–3°, ¹⁰ m. 168°. ¹⁶
(4-EtOC₆H₄NH)₃PS. XXIV. Prisms, m. 152° (from dil. EtOH). ¹⁶
(2-O₂N-4-EtOC₆H₃NH)₃PO. By nitration of the phenetidine derivative. Crystals, m. 126° (from AcOH). ¹⁶
(2-MeC₆H₄NH)₃PO. II.^{77, 110} II (using pyridine). ¹⁰ Needles or plates (from EtOH), m. 236°, ^{77, 110} m. 229–30° (dec.). ¹⁰
(2-MeC₆H₄NH)₃PS. IV. Needles, m. 134.5° (from AcOH). ¹¹⁰
(4-MeC₆H₄NH)₃PO. II.¹¹⁰ II (using pyridine). ¹⁰ XXIV.¹⁶ Prisms (from EtOH), m. 198–9°, ¹⁰ m. 192–4°, ¹⁶ m. 192°. ¹¹⁰
(4-MeC₆H₄NH)₃PS. IV.¹¹⁰ XXIV.¹⁶ Needles, m. 185°, ¹¹⁰ m. 186°. ¹⁶
(2-Me-x-BrC₆H₃NH)₃PO. By bromination of the *o*-tolyl derivative in presence of water. Needles, m. 253° (from AcOH). ¹¹⁰
(2-Br-4-MeC₆H₃NH)₃PO. XXIX. Needles, m. 268°. ⁹²
(4-Me-x-BrC₆H₃NH)₃PO. By nitration of the *p*-tolyl derivative in the presence of water. Needles, m. 221° (from AcOH), ¹¹⁰ m. 222°. ¹⁶
(4-Me-x-O₂NC₆H₃NH)₃PO. By nitration of the *p*-tolyl derivative in acetic acid. Yellow needles, m. 247° (from AcOH). ¹¹⁰
(2,4-Me₂C₆H₃NH)₃PO. II. Needles (from EtOH), m. 225°, ⁶⁴ m. 198°. ⁷⁷
(2,5-Me₂C₆H₃NH)₃PO. II. Crystals, m. 247°. ⁷⁷
(3,4-Me₂C₆H₃NH)₃PO. II. Prisms, m. 183°. ⁷⁷
(2,4,5-Me₃C₆H₂NH)₃PO. II. Needles, m. 217°. ⁷⁷
(1-C₁₀H₇NH)₃PO. II. Needles, m. 216° (from AcOH). ¹¹⁰
(2-C₁₀H₇NH)₃PO. II.¹¹⁰ XXX.²³ Plates, m. 170°, ¹¹⁰ m. 168–70° (from AcOH). ²³
(C₆H₁₁NH)₃PO. II (using pyridine). Crystals, dec. 245–6° (from ligroin). ¹⁰
(C₆H₁₁NH)₃PS. IV. Crystals, m. 143.5–4.5° (from EtOH). ¹⁰
(PhNHNH)₃PO. II.^{86, 129} II (using pyridine). ¹⁰ Needles, dec. 204°, ¹²⁹ m. 196° (from EtOH). ⁸⁶ dec. 185–7°. ¹⁰
(PhNHNH)₃PS. IV. Needles, m. 154° (from EtOAc). ⁸⁶
(4-MeC₆H₄NHNH)₃PO. II. Needles, m. 189°. ⁸⁶

ii. DERIVATIVES OF SECONDARY AMINES

- (Me₂N)₃PO.** II. Liquid, b₁ 76°, *n*_D²⁵ 1.4570. ⁵⁹
(Et₂N)₃PO. II. Liquid. ⁷⁷
(Et₂N)₃PS. IV. XI. Liquid. ⁷⁷
(Pr₂N)₃PO. II. Liquid. ⁷⁷
(iso-Bu₂N)₃PO. II. Liquid. ⁷⁷
(iso-Bu₂N)₃PS. IV. XI. Liquid, *d*₄¹⁵ 0.9965. ⁷⁷
(MePhN)₃PO. II. Needles, m. 162°. ⁷⁷
(EtPhN)₃PO. II. Yellow crystals, m. 182°. ⁷⁷
(C₆H₁₀N)₃PO. II. Plates, m. 75–6° (from Et₂O). ^{77, 83, 94} Mercuric chloride double salt, m. 105°.

314 COMPOUNDS WITH PHOSPHORUS TO NITROGEN BONDS

(C₆H₁₀N)₃PS. IV.^{10,77} XI.^{77,88} Plates (from EtOH), m. 121–2°, ¹⁰ m. 120°.⁷⁷

(C₆H₁₀N)₃PO. II (from tetrahydroquinoline). Prisms, m. 90–1°.⁷⁶

(C₆H₁₀N)₃PS. IV.^{22,75} XI.^{22,75} XVIII.²³ Crystals, m. 192°.⁷⁵ m. 190–2°.²³

(O(CH₂CH₂)₂N)₃PO. II (using pyridine). Crystals, m. 191–2° (from CCl₄).¹⁰

(O(CH₂CH₂)₂N)₃PS. IV. Crystals, m. 145.5–46° (from EtOH).¹⁰

Tri-N-(2-methylindolyl)phosphate. A by-product in the reaction of phosphorus oxychloride with the magnesium derivative of 2-methylindole. Crystals, m. 140–2° (from Et₂O-ligroin). Unstable to hot aqueous alkali.⁹⁶

iii. MISCELLANEOUS COMPOUNDS

o-CICO·C₆H₄N(P(O)(NH·C₆H₄·COCl)₂). IX (from anthranilic acid). Yellow needles, m. 148–53° (from ligroin).¹²¹

B. DERIVATIVES OF AA'A' TYPE

i. DERIVATIVES OF PRIMARY AMINES

(EtNH)(iso-BuNH)₂PS. IV. Needles, m. 48.5°.⁷⁷

(EtNH)(PhNH)₂PO. II. Needles, m. 147° (from dil. EtOH).⁷⁷

(EtNH)(PhNH)₂PS. IV. Needles, m. 106°.⁷⁷

(EtNH)(4-MeC₆H₄NH)₂PS. IV. Crystals, m. 140°.⁷⁷

(EtNH)(PhNHNH)₂PO. II. Crystals, m. 153°.⁷⁷

(PrNH)(PhNH)₂PO. II. Needles, m. 146° (from dil. EtOH).⁷⁷

(PrNH)(PhNH)₂PS. IV. Needles, m. 116°.⁷⁷

(PrNH)(PhNHNH)₂PO. II. Crystals, m. 151°.⁷⁷

(iso-BuNH)(PhNH)₂PO. II. Crystals, m. 207°.⁷⁷

(iso-BuNH)(PhNH)₂PS. IV. Needles, m. 118°.⁷⁷

(iso-BuNH)(4-MeC₆H₄NH)₂PS. IV. Crystals, m. 152°.⁷⁷

(iso-BuNH)(PhNHNH)₂PO. II. Crystals, m. 141°.⁷⁷

(iso-BuNH)(PhNHNH)₂PS. IV. Crystals, m. 129°.⁷⁷

(iso-AmNH)(PhNH)₂PO. II. Crystals, m. 117°.⁷⁷

(iso-AmNH)(4-MeC₆H₄NH)₂PS. IV. Needles, m. 129°.⁷⁷

(iso-AmNH)(PhNHNH)₂PO. II. Crystals, m. 122°.⁷⁷

(Cl₂CH·CONH)(PhNH)₂PO. II. Needles, m. 219–20° (from EtOH).^{123, 124}

(Cl₃C·CONH)(PhNH)₂PO. II. Needles, m. 194–5° (from EtOH).^{123, 124}

(PhNHCH₂·CONH)(PhNH)₂PO. II (from ClCH₂CCl:NPOCl₂). Crystals, m. 156°.²² m. 156° (from EtOH).²²

(Cl₂CH·CONH)(PhNHNH)₂PO. II. Crystals, m. 190° (from EtOH).^{123, 124}

(Cl₃C·CONH)(PhNHNH)₂PO. II. Crystals, m. 237–8° (from EtOH).^{123, 124}

(PhNH)₂(4-O₂NC₆H₄NH)PO. II. Crystals, m. 242°.⁷⁷

(PhNH)₂(3-O₂NC₆H₄NH)PO. II. Crystals, m. 177°.⁷⁷

(2,4-Br₂C₆H₃NH)(PhNH)₂PO. II. Needles, m. 228° (from EtOH).⁷⁷

(PhNH)(3-BrC₆H₄NH)₂PO. XXIX. Needles, m. 165° (from EtOH).⁹²

(PhNH)₂(2-MeC₆H₄NH)PO. II. Prisms, m. 175°.⁹¹

(PhNH)(2-MeC₆H₄NH)₂PO. II. Needles, m. 201°.⁹¹

(PhNH)₂(4-MeC₆H₄NH)PO. II. Scales, m. 168° (from EtOH).⁹¹

(PhNH)(4-MeC₆H₄NH)₂PO. II. Needles, m. 168° (from EtOH).⁹¹

(2,4-Br₂C₆H₃NH)(4-MeC₆H₄NH)₂PO. II. Crystals, m. 214°.⁷⁷

(4-Me-x-O₂N·C₆H₃NH)₂(x-O₂NC₆H₄NH)PO. By nitration of the phenyl-ditolyl derivative in acetic acid. Needles, m. 220° (from AcOH).⁹¹

Diamido 5-(4-hydroxy-2-ethylmercapto-5-imino)pyrimidyl phosphate. II. Green, metallic crystals, dec. 290–300°.⁹¹

(CH₂NH)₂PO(NHPh). II. Insoluble powder, m. 232°.¹²

***o*-C₆H₄(NH)₂PO(NHPh).** II. Crystals, *m.* 214° (from dil. EtOH).¹²

3-Me-1,2-C₆H₃(NH)₂PO(NHC₆H₃-(3 or 4)Me-2-NH₂). IX (from 3,4-diamino-toluene). Needles, *m.* 200° (from dil. EtOH).⁴⁶

PhNH·PO(NHNH)₂PO(NHPh). II. Crystals, *m.* 208–10° (from dil. EtOH).¹⁴

ii. DERIVATIVES OF SECONDARY AMINES

(Me₂N)PO(NHPh)₂. II. Needles, *m.* 196°.⁷⁷

(Me₂N)PS(NHPh)₂. IV. Needles, *m.* 209–10° (from EtOH).⁷⁷

(Me₂N)PO(NHNHPh)₂. II. Crystals, *m.* 194–5°.⁷⁷

(Et₂N)PO(PhNH)₂. II. Needles, *m.* 150°.⁷⁷

(Et₂N)PS(NHPh)₂. IV. Needles, *m.* 192° (from EtOH).⁷⁷

(Et₂N)PO(NHNHPh)₂. II. Crystals, *m.* 184–5°.⁷⁷

(Et₂N)PS(NHNHPh)₂. IV. Crystals.⁷⁷

(Et₂N)PS(NHC₆H₄Me-4)₂. IV. Needles, *m.* 166–7°.⁷⁷

(Et₂N)PO(NC₆H₁₀)₂. II. Liquid.⁷⁷

(Et₂N)PS(NC₆H₁₀)₂. IV. Prisms, *m.* 126°.⁷⁷

(Pr₂N)PO(NHPh)₂. II. Needles, *m.* 220°.⁷⁷

(Pr₂N)PS(NHPh)₂. IV. Plates, *m.* 145° (from ligroin).⁷⁷

(Pr₂N)PO(NHNHPh)₂. II. Needles, *m.* 164°.⁷⁷

(Pr₂N)PS(NHNHPh)₂. IV. Crystals, *m.* 196°.⁷⁷

(Pr₂N)PO(NHC₆H₄Me-4)₂. II. Needles, *m.* 168°.⁷⁷

(iso-Bu₂N)PO(NHPh)₂. II. Needles, *m.* 202°.⁷⁷

(iso-Bu₂N)PO(NHNHPh)₂. II. Crystals, *m.* 168°.⁷⁷

(iso-Bu₂N)PO(NHC₆H₄Me-4)₂. II. Crystals, *m.* 180°.⁷⁷

(iso-Bu₂N)₂(Et₂N)PS. IV. XI. Liquid, *d*₄¹⁵ 1.0023.⁷⁷

(iso-Am₂N)PS(NHPh)₂. IV. Crystals, *m.* 141°.⁷⁷

(MePhN)PO(NHPh)₂. II. Needles, *m.* 192°.⁷⁷

(MePhN)PO(NHNHPh)₂. II. Crystals, *m.* 148°.⁷⁷

(MePhN)PO(NHC₆H₄Me-4)₂. II. Crystals, *m.* 232°.⁷⁷

(MePhN)PO(NC₆H₁₀)₂. II. Crystals, *m.* 86°.⁷⁷

(EtPhN)PS(NHPh)₂. IV. Crystals, *m.* 140°.⁷⁷

(EtPhN)PS(NHC₆H₄Me-4)₂. IV. Crystals, *m.* 158°.⁷⁷

(Ph₂N)PO(NHPh)₂. II. Needles, *m.* 232° (from AcOH).¹⁰¹

(Ph₂N)PO(NHC₆H₄Me-2)₂. II. Plates, *m.* 219° (from EtOH).¹⁰¹

(Ph₂N)PO(NC₆H₁₀)₂. II. Needles, *m.* 200° (from EtOH).¹⁰¹

(C₆H₁₀N)PS(NHPh)₂. IV. Needles, *m.* 199°.⁷⁷

(C₆H₁₀N)PS(NHC₆H₄Me-4)₂. IV. Crystals, *m.* 190°.⁷⁷

(C₆H₁₀N)PS(NHNHPh)₂. IV. Needles, *m.* 158°.⁷⁷

(C₆H₁₀N)₂PS(NHEt). IV. Crystals, *m.* 95°.⁷⁷

(C₆H₁₀N)₂PS(NHBu-iso). IV. Crystals, *m.* 106°.⁷⁷

(C₆H₁₀N)₂PO(NHPh). II. Prisms, *m.* 159°.⁷⁷

(C₆H₁₀N)₂PS(NHPh). IV. Needles, *m.* 112°.⁷⁷

(C₆H₁₀N)₂PO(NHNHPh). II. Crystals, *m.* 155°.⁷⁷

(C₆H₁₀N)₂PO(NHC₆H₄Br-3). II. Crystals, *m.* unstated.⁷⁷

(C₆H₁₀N)₂PO(NHC₆H₄Br-4). II. Needles, *m.* 169° (from EtOH).⁷⁷

(C₆H₁₀N)₂PO(NHC₆H₃Br₂-2,4). II. Crystals, *m.* 186°.⁷⁷

(C₆H₁₀N)₂PO(NHC₆H₄Me-2). II. Needles, *m.* 146°.⁷⁷

(C₆H₁₀N)₂PS(NHC₆H₄Me-4). IV. Crystals, *m.* 157°.⁷⁷

4-((C₆H₁₀N)₂PO(NHC₆H₄))₂SO₂. II. Dimorphic crystals, *m.* 221–2° (from EtOH-Et₂O), and *m.* 190–1° (from CHCl₃-Et₂O).⁵⁰

$(C_9H_{10}N)PO(NHPh)_2$. II (from the tetrahydroquinolyl derivative). Prisms, m. 176° .⁷⁷

F. AMIDES OF PHOSPHONIC AND THIOPHOSPHONIC ACIDS

1. DERIVATIVES OF ALIPHATIC ACIDS

$MePO(NEt_2)_2$. XV. Liquid, b_{22} $145-8^\circ$.⁷⁷

$MePO(NPr_2)_2$. XV. Liquid, b_{25} $176-80^\circ$.⁷⁷

$MePO(NC_5H_{10})_2$. XV. Obtained as a crystalline adduct with ethanol.⁷⁷

$ClCH_2CH_2PO(NHPh)(OCH_2CH_2Cl)$. II. Needles, m. $95.5-97^\circ$ (from dil EtOH).⁸⁸

$ClCH_2CH_2PO(NHPh)_2$. II. Crystals, m. $169-70^\circ$ (from benzene).⁸⁸

$BrCH_2CH_2PO(NHPh)_2$. II. Crystals, m. $169-70^\circ$ (from dil EtOH).¹⁰⁹

$CH_2:CMc \cdot PO(NMe_2)_2$. II. Liquid, b_{2-3} $76-80^\circ$, n_D^{20} 1.4735.⁴³

iso-BuPS(NHNHPh)₂. IV. Plates, m. 128° .⁴²

iso-AmPO(NHNHPh)₂. II. Powder, m. $134-5^\circ$ (from dil EtOH).⁴²

$MeC:CH \cdot CMe_2 \cdot P(O)(NHPh)O$. Probable structure of the reaction product of Michaelis' "diacetonephosphoryl chloride" and aniline. Crystals, m. $122-5^\circ$ (from dioxane).¹

2. DERIVATIVES OF AROMATIC ACIDS

$PhPO(NH_2)_2$. II. Plates, m. 189° (from EtOH).⁷⁴

$PhPO(NHPh)OH$. III. Crystals, m. 125° .⁷⁴ Obtained only in very crude state by XXXI (using water).⁷⁸

$PhPO(NHPh)(OEt)$. XXXI. Crystals, m. 105° .⁷⁸

$PhPO(NHPh)(OPh)$. X. Crystals, m. 63° , b_{25} 235° .⁷⁴

$PhPO(NHPh)_2$. II.⁷⁴ XXXI (using aniline).⁷⁸ Needles, m. 211° (from EtOH).

$PhPO(NHPh)(NHC_6H_4Me-4)$. XXXI (from *p*-toluidine).⁷⁸ Needles, m. 200° .

$PhPO(NHC_6H_4Me-4)_2$. III (with rapid heating). Crystals, m. 220° .⁷⁸

$PhPO(NHPh)(NC_5H_{10})$. XXXI (using piperidine). Needles, m. 212° .⁷⁸

$PhPO(NC_5H_{10})_2$. II. XIII. Crystals, m. 86° .⁸⁸

$PhPS(NC_5H_{10})_2$. XI. Needles, m. 92° (from Et₂O).⁸⁸

$PhPO(NC_9H_{10})_2$. II (from tetrahydroquinoline). Crystals, m. 216° .⁷⁸

$PhPO(NHNHPh)_2$. II. Crystals, m. 175° (from EtOH).⁷⁴

$PhPO(NHPh) \cdot PhN \cdot PO(Ph)OH$. XXXI (using water). Crude, m. 190° .⁷⁸

$4-BrC_6H_4PO(NH_2)_2$. II. Plates, m. 202° (from EtOH).⁸⁶

$4-H_2NC_6H_4PO(NH_2)_2$. By heating the above substance with ammonium hydroxide and cuprous oxide on a steam bath. Crystals, m. 224° , isolated by neutralization of solution in mineral acid.⁸⁶

$4-PhNHC_6H_4PO(NHPh)_2$. II (using the *p*-chloroformyl derivative). Crystals, m. 242° .⁷⁴

$2-MeC_6H_4PO(NHPh)_2$. II. Needles, m. 234° .⁷⁴

$4-MeC_6H_4PO(NHPh)OH$. III-XXIII.⁷⁴ XXXI (using dilute NaOH).⁷⁸ Needles, m. 150° . XXXI, using acetic anhydride, yields the acetyl derivative, m. 162° (from water).⁷⁸

$4-MeC_6H_4PO(NHC_6H_4Me-4)OH$. III-XXIII. Crystals, m. 208° .⁷⁴

$4-MeC_6H_4PO(NHPh)(OMe)$. XXXI (using methanol). Crystals, m. 65° .⁷⁸

$4-MeC_6H_4PO(NHC_6H_4Me-4)(OEt)$. XXXI (using ethanol). Crystals, m. 53° .⁷⁸

$4-MeC_6H_4PO(NH_2)(OPh)$. II. Crystals, m. $115-6^\circ$ (from Et₂O).⁷⁴

$4-MeC_6H_4PO(NHPh)(OPh)$. X. Crystals, m. 59° , b_{48} 283° .⁷⁴

$4-MeC_6H_4PO(NHC_6H_4Me-4)(OPh)$. X. Crystals, m. 48° , b_{33} 280° .⁷⁴

$4-MeC_6H_4PO(NHNHPh)(OPh)$. II. Needles, m. $173-4^\circ$.⁷⁴

- 4-MeC₆H₄PO(NC₆H₁₀)(OPh).** II. Liquid.⁷⁴
4-MeC₆H₄PO(NH₂)₂. II. Crystals, m. 209° (from EtOH).⁷⁴
4-MeC₆H₄PO(NHPh)₂. XXXI (using aniline). Needles, m. 209° (from EtOH).⁷⁸
4-MeC₆H₄PO(NHPh)(NHC₆H₄Me-4). XXXI (using aniline). Needles, m. 221°. ⁷⁸
4-MeC₆H₄PO(NHC₆H₄Me-4)₂. II.⁷⁴ XXXI (using *p*-toluidine).⁷⁸ Needles, m. 237°. ^{74, 78}
4-MeC₆H₄PO(NHNHPh)₂. II. Needles, m. 171°. ⁷⁴
4-MeC₆H₄PO(NC₆H₁₀)₂. II. Needles, m. 60°. ⁸⁰
4-MeC₆H₄PS(NC₆H₁₀)₂. IV. XI.⁸⁰ Crystals, m. 88°. ⁸⁰
4-MeC₆H₄PO(NC₆H₁₀)₂. II (from tetrahydroquinoline). Needles, m. 181°. ⁷⁸
4-MeC₆H₄PO(OH)·PhN·PO(C₆H₄Me-4)(NHPh). XXXI (using water). Crystals, m. 152°. ⁷⁸
2,4,5-Me₃C₆H₂PO(NHPh)₂. II. Needles, m. 197°. ⁷⁴
2,4,5-Me₃C₆H₂PO(NHNHPh)₂. II. Needles, m. 208°. ⁷⁴
(PhCH₂)₂CH·PO(NH₂)OH. II-XXIII. Plates, m. 244°. ⁷⁹ Silver salt.⁷⁹
(PhCH₂)₂CH·PO(NHPh)₂. II. Needles, m. 196° (from dil. EtOH). ⁷⁹
(PhCH₂)₂CH·PO(NHNHPh)₂. II. Needles, m. 164° (from EtOH). ⁷⁹
(Me)(Ph)PO(NHPh). II. Needles, m. 142° (from EtOAc-ligroin). ⁸⁸
Ph₂PO(Net₂). XVII. Crystals, m. 138° (from Et₂O). ⁷⁷
(4-MeC₆H₄)₂PS(NH₂). IV (requires prolonged heating to 160–70°). Crystals, m. 139° (from dil. EtOH). ⁷⁶
(4-MeC₆H₄)₂PS(NHPh). IV (see note above). Needles, m. 152° (from EtOH). ⁷⁶
(4-MeC₆H₄)₂PS(NHNHPh). IV. Needles, m. 135.5° (from EtOH). ⁷⁶
(4-MeC₆H₄)₂PS(Net₂). IV. Crystals, m. 177–8° (from water). ⁷⁶
(4-MeC₆H₄)₂PS(NC₆H₁₀). IV. Needles, m. 134° (from EtOH). ⁷⁶
3-Camphorylene-methanephosphonodianilide. II. Needles, m. 227–8°. ⁷⁹
3-Camphorylene-methanephosphonodi-*p*-toluidide. II. Crystals, m. 210°. ⁷⁹
3-Camphorylene-methanephosphonodi-*p*-phenetide. II. Needles, m. 137°. ⁷⁹

G. COMPOUNDS WITH ACTUAL OR POTENTIAL UNSATURATED PHOSPHORUS-NITROGEN BONDS

1. IMIDES OF PHOSPHONOUS ACIDS

- PhP:N·NHPh.** II. Plates, m. 152° (from EtOAc). ⁸⁶
PhP:N·NHC₆H₄Me-4. II. Crystals, m. 162°. ⁸⁸
PhP:N·NPh(CH₂Ph). II. Crystals, m. 141° (from CHCl₃-Et₂O). ⁸⁶
4-ClC₆H₄P:N·NHPh. II. Crystals, dec. 161° (from benzene). ⁷⁴
4-BrC₆H₄P:N·NHPh. II. Crystals, m. 160° (from benzene). ⁷⁴
4-EtC₆H₄P:N·NHPh. II. Crystals, m. 139°. ⁷⁴
2,4,6 Me₃C₆H₂P:N·NHPh. II. Crystals, m. 135° (from Et₂O). ⁷⁴

2. PHOSPHINIMINES AND RELATED COMPOUNDS

- Et₃P:NH.** XXXII. Isolated as the hydrazoic acid salt: crystals (from water), which explode on heating. ¹¹⁹
Et₃P:NMe. XXXII (from methylazide, in the cold). Liquid, b₁₁ 94–6°. ¹¹⁹
Et₃P:NEt. XXXII. Liquid, b₁₁ 93.5°. ¹¹⁹
Et₃P:NPh. XXXII. Liquid, b_{0.08} 116°. ¹¹⁹
Et₃P:N·COPH. XXXII. Crystals, m. 62.5–63°. ¹¹⁹
iso-Am₃P:NEt. XXXII. Liquid, b_{0.23} 119°. ¹¹⁹
iso-Am₃P:NPh. XXXII (from the phosphazide). Liquid, b_{0.04} 161°. ¹¹⁹
Et₃PhP:NPh. XXXII. Crystals, m. 69–70°. ¹¹⁹

- Et₂PhP:N·COPh.** XXXII.¹¹⁹ Crystals, m. 73–4°.
- Ph₃P:NMe.** XXXII. Crystals, m. 62–5°.¹¹⁹
- Ph₃P:NEt.** XXXII. Crystals, m. 90°. Ethiodide, m. 164–5°.¹¹⁹
- Ph₃P:N·COPh.** XXXII. Crystals, m. 193–4°.¹¹⁹
- Ph₃P:NPh.** XXXII. Crystals, m. 131–2°.¹¹⁹
- Ph₃P:NC₆H₄Me-4.** XXXII. Crystals, m. 134–5° (from Et₂O).¹¹⁹
- Ph₃P:NC₆H₃Me₂-2,4.** XXXII. Crystals, m. 130–1°.¹¹⁹
- Cyanuro-monoazide-di-(triphenylphosphinimine).** XXXII. Crystals, m. 243° (dec.).⁸⁴
- Cyanuro-tri-(triphenylphosphinimine).** XXXII (from the above compound on heating with triphenylphosphine). Needles, m. 239° (from xylene).⁸⁴
- Et₃P:N:N:C(C₆H₄-o)₂.** XXXII (from diazofluorene). Crystals, m. 160° (from dry benzene). Methiodide, m. 109–13°.¹²¹
- Et₃P:N:N:CPh₂.** XXXII. Unstable yellow solid.¹²¹
- Et₂PhP:N:N:CPh₂.** XXXII. Yellowish unstable solid, m. 113°.¹²¹
- Ph₃P:N:N:CPh₂.** XXXII. Crystalline powder, dec. 173°.¹²¹
- Ph₃P:N:N:CHCO₂Et.** XXXII. Crystals, m. 113–4° (from benzene-Et₂O).¹²¹
- Et₂PhP:N:N:C(C₆H₄-o)₂.** XXXII. Crystals, m. 115°.¹²¹
- Ph₃P:N:N:C(C₆H₄-o)₂.** XXXII. Yellow crystals, m. 204–5°.¹²¹ On recrystallization (from EtOH), m. 209–10°.¹²¹
- iso-Am₃P:N:N:NPh.** XXXII. Crystals, m. 57–8°; poorly stable.¹¹⁹
- Et₂PhP:N:N:NPh.** XXXII. Crystals, dec. 51–2°.¹¹⁹
- Ph₃P:N:N:NC₁₀H₇-1.** XXXII. Crystals, dec. 63.5°, to Ph₃P:NC₁₀H₇-1, which forms crystals, m. 141–3°.¹¹⁹
- 4-ClCOC₆H₄·SO₂:N:PCl₃.** XXXII (from *p*-sulfamylbenzoic acid and PCl₅). Prisms, m. 82°; poorly stable.¹⁰⁷
- Et₃P:N·SO₂·C₆H₄Me-4.** XXXII. Crystals, m. 119°.⁷¹
- Pr₃P:N·SO₂·C₆H₄Me-4.** XXXII. Crystals, m. 66°.⁷¹
- Bu₃P:N·SO₂·C₆H₄Me-4.** XXXII. Crystals, m. 54°.⁷¹
- Et₂PhP:N·SO₂·C₆H₄Me-4.** XXXII. Crystals, m. 82°.⁷¹
- Ph₃P:N·SO₂·C₆H₄Me-4.** XXXII. Crystals, m. 187°, obtained with dry Chloramine-T. The hydrated form yields the complex amido derivative, (4-MeC₆H₄-SO₂NH·PPh₃)₂NSO₂C₆H₄Me-4, m. 138°.⁷¹
- (2-MeOC₆H₄)₃P:N·SO₂·C₆H₄Me-4.** XXXII. Crystals, m. 273–4°; hydrate, crystals, m. 149°.⁷¹
- (3-MeOC₆H₄)₃P:N·SO₂·C₆H₄Me-4.** Isolated only as the hydrate. XXXII. Crystals, m. 112°.⁷¹
- (4-MeOC₆H₄)₃P:N·SO₂·C₆H₄Me-4.** XXXII. Crystals, m. 155°; hydrate, crystals, m. 121°.⁷¹
- (2-ClC₆H₄)₃P:N·SO₂·C₆H₄Me-4.** XXXII. Crystals, m. 235–6°.⁷¹
- (4-ClC₆H₄)₃P:N·SO₂·C₆H₄Me-4.** XXXII. Crystals, m. 232°; hydrate, crystals, m. 115–6° (crude).⁷¹
- (2-MeC₆H₄)₃P:N·SO₂·C₆H₄Me-4.** XXXII. Crystals, m. 188°.⁷¹
- (3-MeC₆H₄)₃P:N·SO₂·C₆H₄Me-4.** Isolated only as the hydrate; XXXII. Crystals, m. 98°.⁷¹
- Et₂(4-MeC₆H₄)₂P:N·SO₂·C₆H₄Me-4.** XXXII. Crystals, m. 120°.⁷¹
- (4-MeC₆H₄)₂P:N·SO₂·C₆H₄Me-4.** XXXII. Crystals, m. 174°; hydrate, crystals, m. 106°.⁷¹
- (2-C₆H₄N)₃P:N·SO₂·C₆H₄Me-4.** XXXII. Crystals, m. 177° (from EtOH).⁷³

3. IMIDOPHOSPHITES

Note. The monomer formulas are illustrated below. The actual state of aggregation is probably dimeric, with ring formation.

PhN:PCl. VIII. Prisms (from benzene), m. 136–7°. ⁸⁹

PhN:POEt. By the reaction of sodium ethoxide with the above. Liquid. ⁸⁹

PhN:POPh. As above, using sodium phenoxide. Prisms, m. 189–90°. ⁸⁹

PhN:POCH₂Ph. As above, using PhCH₂ONa. Crystalline solid. ⁸⁹

PhN:PNHPh. VIII. By heating the above chloride with aniline. ^{41, 89} Crystals, m. 251–3°. ⁴¹ Dimeric mol. wt. ⁴¹ Hydrate, m. 152–3°. ⁸⁹

2-MeOC₆H₄N:PNHC₆H₄OMe-2. VIII. Crystals, m. 138–40°. Dimeric mol. wt. ⁴¹

4-MeC₆H₄N:PNHC₆H₄Me-4. VIII. Crystals, m. 197–200°. ⁴¹

4. DERIVATIVES RELATED TO PHOSPHONITRILE

(PhNH)₂PN. By heating PNC₂ with aniline. Needles, m. 268° (from AcOH). ¹¹³

The reactions of PNC₂ have not been adequately explored to date. The above is only one of possible reaction products.

PhN:PCl₃. IX (using aniline hydrochloride). Colorless sublimate. ³⁷

PhN:P(NHPh)₃. XII (using water, followed by alcoholic KOH). Needles, m. 232° (from EtOH). Treatment with aqueous solvents yields (PhNH)₃PO. ⁸²

2-MeC₆H₄N:P(NHC₆H₄Me-2)₃. The product could not be obtained by XII, because of side reactions. ⁸³

5. IMIDOPHOSPHATES AND IMIDOTHIONOPHOSPHATES

Note. The monomer formulas are listed below. Determinations of the molecular weights of several of these substances indicate dimer formation, probably with cyclization. (See text.)

EtN:P(S)NHEt. VIB. Prisms, m. 169° (from Et₂O). Mol. wt. dimeric. ⁷⁸

PrN:P(O)NHPr. VIA. Needles, m. 213° (from CHCl₃). Mol. wt. near monomer. ⁷⁸

PrN:P(S)NHPr. VIB. Prisms, m. 152° (from Et₂O). Mol. wt. dimeric by freezing point method, monomeric by boiling point method. ⁷⁸

iso-BuN:P(O)NHBu-iso. VIA. Needles, m. 271° (from CHCl₃). Mol. wt. nearly monomeric. ⁷⁸

iso-BuN:P(S)NHBu-iso. VIB. Prisms, m. 150° (from Et₂O). Mol. wt. dimeric by freezing point method, monomeric by boiling point method. ⁷⁸

iso-AmN:P(O)NHAm-iso. VIA. Resin. ⁷⁸

iso-AmN:P(S)NHAm-iso. VIB. Needles, m. 90° (from Et₂O). ⁷⁸

PhCH₂N:P(S)NHCH₂Ph. VIB. Crystals, m. 197–9°. Dimeric mol. wt. ⁸³

PhN:P(O)Cl. VID. Needles (from EtOH) or prisms (from CHCl₃-Et₂O), m. 228°. Mol. wt. dimeric. Reaction with an excess of sodium phenoxide yields PhNHP(O)(OPh)₂, whereas a deficient amount yields PhN(PO(OPh)₂)(PO(NHPh)(OPh)), m. 185°. ⁷⁸

PhN:P(S)Cl. VIG. Needles, m. 149° (from benzene), b₈₀ 280–90°. ⁸¹

PhN:P(S)OEt. By reaction of the above chloride with sodium ethoxide. Crystals, m. 206° (from EtOH). ⁸¹

PhN:P(O)OC₆H₄CO₂Ph-2. VID (using *o*-PhO·CO·C₆H₄OPOCl₂). Crystals, m. 152° (from EtOH). ⁸³

PhN:P(O)NHPh. XII yields fairly pure monomer. Needles, m. 225–6° (from EtOH). ³⁷ VIA, ^{78, 82} best done in vacuo. ^{85, 92} VIC. ^{78, 92} VID. ^{77, 78} These procedures

320 COMPOUNDS WITH PHOSPHORUS TO NITROGEN BONDS

yield a product with dimer mol. wt. Powder, m. 357-9°, ⁷⁶ m. 357°, ⁷⁸ m. 320-5°. ¹⁰⁰
Insoluble in usual solvents.

PhN:P(S)NHPh. VIB.²³ VIG.⁸¹ Needles, m. 233-5°, ²³ m. 226-7° (from EtOH).⁸¹
Apparently dimeric.

PhN:P(O)NC₆H₁₀. VID (from C₆H₁₀NPOCl₂). By heating dimeric PhN:PCl with piperidine. Plates, m. 233° (from EtOH). Mol. wt. dimeric.⁷⁸

PhN:P(O)NMePh. VIA. VID (from MePhNPOCl₂). Needles, m. 234° (from EtOH).⁷⁸

3-BrC₆H₄N:P(O)NHC₆H₄Br-3. VIA (from (RNH)₂(PhNH)PO). VID. Powder, m. 329°; forms an adduct with ethanol, m. 203°. ⁹²

4-ClC₆H₄N:P(S)Cl. VIG. Crystals, m. 188° (from benzene), b₁₆ 230°. ⁸¹

4-ClC₆H₄N:P(S)OEt. By reaction of the above compound with sodium ethoxide. Crystals, m. 91° (from EtOH).⁸¹

4-ClC₆H₄N:P(O)NHC₆H₄Cl-4. VIC. Needles, m. above 300° (from AcOH).¹⁰¹

4-Cl-2(or 3)-O₂N·C₆H₃N:P(O)NHC₆H₃-4-Cl-2(or 3)-NO₂. By nitration of the above compound in acetic acid. Yellow needles, m. above 300° (from AcOH).¹⁰¹

2,4-Cl₂C₆H₃N:P(O)NHC₆H₃Cl₂-2,4. VID. Crystalline solid. ⁹²

2-MeC₆H₄N:P(S)Cl. VID. Needles, m. 260° (from benzene), b₂₈ 290°. ⁸¹

2-MeC₆H₄N:P(S)OEt. By reaction of the above compound with sodium ethoxide. Needles, m. 176° (from benzene).⁸¹

2-MeC₆H₄N:P(S)OC₆H₄Me-2. As above, using sodium cresoxide. Powder, m. 247°. ⁸¹ Corresponding phenoxy derivative, m. 236°. ⁸¹

2-MeC₆H₄N:P(S)NHC₆H₄Me-2. As above, using *o*-toluidine. Powder, m. 258°. ⁸¹

2-MeC₆H₄N:P(S)NHPh. As above, using aniline. Powder, m. 162°. ⁸¹

2-MeC₆H₄N:P(O)NHC₆H₄Me-2. VIA. VID. Crystals, m. 309°; insoluble. ⁹²

2-MeC₆H₄N:P(O)NMePh. VID. Plates, m. 191°. ⁷⁸

2-MeC₆H₄N:P(O)NC₆H₁₀. VIA (with elimination of toluidine). VID. Crystals, m. 195° (from Et₂O).⁷⁸

2-MeC₆H₄N:P(S)NC₆H₁₀. By reaction of piperidine with the corresponding chloro derivative. Powder, m. 236°. ⁸¹

4-MeC₆H₄N:P(O)Cl. VID. Needles, m. 336° (from benzene). Mol. wt. dimeric. ⁷⁸

4-MeC₆H₄N:P(S)Cl. VIG. Prisms, m. 170° (from benzene).⁸¹

4-MeC₆H₄N:P(S)OEt. From the above compound and sodium ethoxide. Crystals, m. 176° (from Et₂O).⁸¹

4-MeC₆H₄N:P(O)NHC₆H₅(?). By-product of reaction of RNHPOCl₂ with R'NH₂. Needles, m. 188° (from dil. EtOH). Apparently monomeric. ⁹⁷

4-MeC₆H₄N:P(O)NHC₆H₄Me-2. VID. Crystals, m. 309°. ⁷⁸

4-MeC₆H₄N:P(O)NHC₆H₄Me-4. XII. Needles, m. 226-8°; apparently a monomer. ⁹⁷ VID. VIC. These procedures yield the dimeric form: powder, m. 328°, insoluble in usual solvents. ^{78, 92}

4-MeC₆H₄N:P(S)NHC₆H₄Me-4. From the corresponding chloro derivative and *p*-toluidine. Yellow powder, m. 182°. ⁸¹

4-MeC₆H₄N:P(O)NMePh. VID. Plates, m. 251°. ⁷⁸

4-MeC₆H₄N:P(O)NC₆H₁₀. VID. Crystals, m. 294° (from EtOH).⁷⁸

4-MeC₆H₄N:P(S)NC₆H₁₀. From the corresponding chloro derivative and piperidine. Crystals, m. 275°. ⁸¹

4-Me-2-BrC₆H₃N:P(O)NHC₆H₃-2-Br-4-Me. VID. Crystalline solid. ⁹²

2,4,5-Me₃C₆H₂N:P(S)Cl. VIG. Needles, m. 257° (from benzene).⁸¹

2,4,5-Me₃C₆H₂N:P(S)OEt. From the above compound and sodium ethoxide. Needles, m. 201° (from EtOH).⁸¹

2,4,5-Me₃C₆H₂N:P(O)NHC₆H₂Me₃-2,4,5. VID. Crystals, m. 217°. ⁹²

2,4,6-Me₃C₆H₂N:P(O)NHC₆H₂Me₃-2,4,6. VID. Needles, m. 240° (from EtOH).⁹²
Ph·CO·N:P(O)NHPh or PhN:P(O)NH·CO·Ph. II (from Ph·CO·NHPOCl₂ and aniline). Modified XII (from (PhNH)(Ph·CO·NH)POCl and aniline). Needles, m. 226° (from EtOH).¹³⁰

PhNH P(O):N CPh:NPh. XXI (from benzamide); II (with aniline). Needles, m. 227-8° (from EtOH).¹³⁰

6. PHOSPHONOIMIDES

PhP(O):NPh. VIE. VIF. Prisms, m. 290° (from CHCl₃), b. above 360° in vacuo. Mol. wt. dimeric (boiling point method).⁷⁸

PhP(O):NC₆H₄Me-2. VIE. Crystals, m. 220°. ⁷⁸

PhP(O):NC₆H₄Me-4. VIE. Crystals, m. 380°. ⁷⁸

PhP(O):NC₆H₄Me₃-2,4,5. VIE. Prisms, m. 280° (from benzene).⁷⁸

4-MeC₆H₄P(O):NPh. VIE. Plates, m. 273° (from benzene).⁷⁸

4-MeC₆H₄P(O):NC₆H₄Me-2. VIE. Crystals, m. 262° (from benzene-ligroin).⁷⁸

4-MeC₆H₄P(O):NC₆H₄Me-4. VIE. VIF. Powder, m. 312°. ⁷⁸

7. MISCELLANEOUS COMPOUNDS

PhC:N·NPh·P(O)(NPh·NH·COPh)O. IX (from benzoyl-phenyl-hydrazine, by treatment with PCl₅ in ether, followed by action of moisture). Prisms, m. 164.5° (from EtOH).¹⁰²

PhC:N·NPh·P(O)(OH)O. By treatment of the ether extract in the above preparation with cold methanol. Needles, m. 161° (from MeOH).¹⁰²

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Quasi-Phosponium Compounds

The substances that are the subject of this chapter may be regarded as variants of the usual phosphonium compounds, R_4PX , in which one or more radicals R are replaced by ester groups, OR , or amido groups, RNH or R_2N , or as variants of the polyhalides, R_4PX_4 , R_2PX_3 , and R_3PX_2 , in which radicals R are similarly substituted. Although very few of these compounds have been isolated in the pure state, it is very likely that substances of this general type are the transient intermediates in many of the common reactions of organophosphorus compounds, intermediates that yield the final products upon decomposition in a manner analogous to that of the conventional quaternary derivatives.

METHODS OF PREPARATION

The following methods are principally used for the (O)-series.

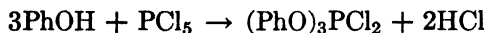
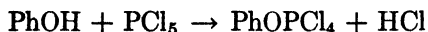
I. Addition of halogen to phosphites

Although the alkyl phosphites are capable of halogen addition, the products suffer cleavage at ordinary temperatures. The aromatic esters are able to retain the quasi-phosponium structures, although mild conditions have to be used to prevent decomposition of the products. Thus passage of chlorine into a solution of the corresponding phosphite or halophosphite in an inert solvent, with cooling, results in the formation of the series of aryloxyphosphorus chlorides.^{1,2,3} The products are isolated by careful evaporation.



II. Reaction of phenols with phosphorus pentahalides

Phenols react with phosphorus pentachloride, on mild heating to form products of higher degrees of substitution, yielding a series of aryloxyphosphorus chlorides, the structural composition of which depends upon the ratio of the reagents used.^{3,7} For example,



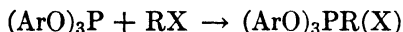
Reaction of phenols with the aryloxyphosphorus chlorides may be used also, in the same sense, and a few very unstable penta-aryloxy derivatives have been obtained in this manner.³



Dihydroxy phenols, such as catechol, react similarly and yield the corresponding cyclic derivatives, such as $1,2\text{-C}_6\text{H}_4\text{O}_2\text{PCl}_3$.³

III. Reaction of tertiary phosphites or of esters of phosphonous or phosphinous acids with alkyl halides

This reaction when used with the aliphatic phosphites results in the spontaneous cleavage of the primary adduct, which is a quasi-phosphonium compound. In the aryl phosphite series the adducts, often quite stable to moderate heating, may be isolated by evaporation of any volatile solvents or excess of reagents from the reaction mixture, which had been kept for several hours at a suitable temperature: about 100° for addition of methyl iodide, 200° for ethyl iodide,²⁰ and 175° for benzyl chloride.¹⁷ The reaction with tertiary phosphites is shown as follows:



The other trivalent phosphorus esters behave similarly. Thus esters of phosphonous acids, $\text{RP}(\text{OR})_2$, give quasi-phosphonium compounds $\text{RR}'\text{P}(\text{OR})_2\text{X}$, whereas esters of phosphinous acids, $\text{R}_2\text{P}(\text{OR})$, give $\text{R}_2\text{R}'\text{P}(\text{OR})\text{X}$ derivatives.^{16, 22}

The following methods are used for the (N)-series.

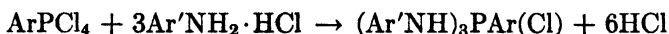
IV. Reaction of amines with phosphorus pentachloride

This reaction is a nitrogen counterpart of the reaction of phenols shown in Section II. When an excess of a primary amine, usually aromatic, is heated with phosphorus pentachloride, the final reaction products are tetra-amidophosphorus chlorides, $(\text{RNH})_4\text{PCl}$.^{9, 11, 14} These substances are very similar to true quaternary phosphonium compounds, and the ionic chlorine may be replaced by other groups by usual metathesis. Amine hydrochlorides may be used instead of the free amines. The reaction requires fairly high temperatures for the completion of tetrasubstitution, although it is very vigorous in the first stages.



When a secondary amine is allowed to react with phosphorus pentachloride, the primary products are adducts of the primary (N)-quasi-phosphonium tetrachloride with phosphorus pentachloride, $R_2NPCl_4 \cdot PCl_5$.

Substitution of arylphosphorus halides for the pentachloride yields in a similar manner the quasi-phosphonium compounds that have radicals R bound directly to the phosphorus atom.²¹ The monohalides so obtained are readily converted to the corresponding hydroxides on treatment with alkali.²¹



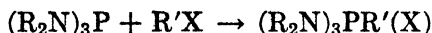
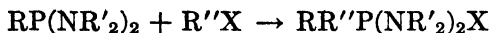
V. Addition of acids to imidoamidophosphates

Reactions of this type have been explored but little. Thus warming arylamido-arylimidophosphates with organic acids yields the corresponding acyl derivatives of the quaternary (N)-derivatives.¹⁴



VI. Addition of alkyl halides to amides of trivalent phosphorus

This method is the nitrogen counterpart of the reactions cited in Section III. Amides of secondary amines based on trivalent phosphorus, that is, $(R_2N)_3P$ compounds, diamides of phosphonous acids, as well as the ester amides of these categories, readily add alkyl halides, such as methyl iodide and benzyl chloride, under conditions given in Section III.^{18, 23} The products are quaternary (N)-quasi-phosphonium halides; for example,

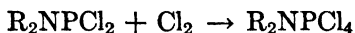


The halides may be converted to the hydroxides by means of moist silver oxide, in a manner analogous to that used with true phosphonium compounds.^{15, 17, 24} It is interesting to note that in reactions in which ester amides are used, the ester radical OR may be displaced by halogen to yield a dihalide instead of the monohalide; this appears to occur with the phenyl esters only.¹⁷

VII. Addition of halogen to amidodihalophosphites

Amidodichlorophosphites based on secondary amines, that is, compounds of the general type R_2NPCl_2 , readily add chlorine to form the tetrachlorides. The reaction is conducted similarly to the procedure

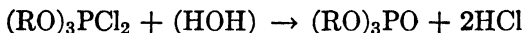
given in Section I.¹⁷ Primary amine derivatives cannot be used satisfactorily because of the halogen attack on the free hydrogen atoms.



GENERAL CHARACTERISTICS

Substances in this family are usually rather unstable products that suffer decomposition by the thermal or hydrolytic routes in a manner strongly reminiscent of the true phosphonium compounds. The characteristics of the ester structures are also superimposed on the behavior of the compounds with OR groups, whereas the characteristics of phosphine polyhalides are evident in compounds with a plurality of halogen atoms.

Hydrolysis of the polyhalides of the (O)-type yields the corresponding phosphates.^{2, 3, 4, 7, 25}



Disproportionation often accompanies such hydrolyses. Thus phenoxyphosphorus tetrachloride yields some triphenyl phosphate.⁴

Whereas reactions with phenols generally lead to progressive displacement of halogen atoms by the aryloxy groups,³ alcohols usually react in such a manner that two halogen atoms are replaced by a semipolar oxygen, with elimination of alkyl halide. Reactions of type indicated here probably result from thermal decomposition of the quaternary halide, $(\text{ArO})_3(\text{RO})\text{PX}$, and are often used in the conversion of phosphites into phosphates. A partial displacement of the aryl radicals by alkyls may occur at the higher temperatures.^{2, 3, 25}

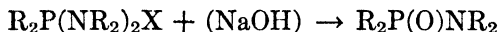
Derivatives with at least two halogen atoms in the molecule react smoothly with sulfur dioxide, with replacement of two halogen atoms by semipolar oxygen.^{1, 2, 3}

Purely thermal decomposition of the (O)-type halides results in the elimination of aryl halide. Phenoxy derivatives suffer this change, beginning at 180°, whereas the *p*-cresyl derivatives are cleaved at 200°; naphthyl derivatives require higher temperatures, about 300°.⁷

Reactions with amines cause progressive replacement of the available halogen atoms (except the last one) by the corresponding amine radicals.^{2, 3, 7} Transposition of the aryl group may occur simultaneously along with substitution and decomposition reactions. Thus triphenoxyphosphorus dichloride reacts with aniline to form diphenyl *N*-phenylamidophosphate and diphenylamine.^{2, 3, 7}

The quaternary (N)-type monohalides based on primary amines, that is, compounds $(\text{RNH})_4\text{PX}$, as mentioned earlier, behave much like the true quaternary phosphonium compounds, with metathetically replaceable halide, which is essentially ionic.^{9, 11, 14} The hydroxides of these substances are essentially neutral substances.¹⁵ Thermal decomposition of the halides yields phosphoric amides, $(\text{RNH})_3\text{PO}$, with elimination of amine salt.¹²

Substances in which one or more radicals are carbon-phosphorus-bound react with warm alkali in a manner analogous to the reaction of quaternary halides. Naturally, the cleavage that takes place does not affect the carbon-phosphorus bond. The loss of the oxygen- or nitrogen-bound radicals produces esters or amides of the corresponding phosphonic acids.^{18, 20}



QUASI-PHOSPHONIUM COMPOUNDS

(O)-TYPE

PhOPCl₄. I. Unstable hygroscopic needles.^{1, 2}

PhOPCl₂Br₂. I. Very unstable solid.²

(4-MeC₆H₄O)PCl₄. I. Unstable solid.⁴

(PhO)₂PCl₃. I. Unstable crystals.²

(PhO)₂PClBr₂. I. Unstable orange solid.²

1,2-C₆H₄O₂PCl₃. II. Needles, m. 61–2°. ³

1,2-(4-MeC₆H₃)O₂PCl₃. I. Liquid, b₁₁ 158°. ⁶

(PhO)₃PCl₂. I.^{2, 3} II.⁷ Liquid. Decomposes to chlorobenzene at 200°.

(PhO)₃PBr₂. I. Reddish plates.²⁵

(2-MeC₆H₄O)₃PCl₂. II. Liquid. Decomposes to *o*-chlorotoluene at 180°. ⁷

(3-MeC₆H₄O)₃PCl₂. I. II. Liquid. Decomposes to *m*-chlorotoluene. ⁷

(4-MeC₆H₄O)₃PCl₂. I. II. Liquid. Decomposes to *p*-chlorotoluene. ⁷

(2-Cl₂CH·C₆H₄O)₃PCl₂. I. Liquid, obtained only in crude state. ²⁷

(1-C₁₀H₇O)₃PCl₂. I. Green oil. ⁵

(1-C₁₀H₇O)₃PBr₂. I. Red liquid. ⁵

(2-C₁₀H₇O)₃PCl₂. I.⁵ II.⁷ Liquid. Decomposes at 310° to 2-chloronaphthalene. ⁷

(2-C₁₀H₇O)₃PBr₂. I. Dark liquid. ⁵

(2-(1,6-Br₂C₁₀H₅)O)₃PCl₂. II. Hygroscopic liquid. ⁵

(1,2-C₆H₄O)₂PCl₂. II. Needles, m. 166–8°, b₁₁ 194°. ³ A dimer of this substance is obtained similarly if the reaction is conducted slowly; crystals, dec. 180°. ³

(1,2-(4-MeC₆H₃)O)₂PCl. II. Hygroscopic solid. ⁶

(PhO)₅P. II. Very hygroscopic plates, m. 46–52°. ³

(PhO)₃(1,2-C₆H₄O)₂P. II. Plates, m. 95–107°. ³

(PhO)(1,2-C₆H₄O)₂P. II. Plates, m. 192°, b₁₀₋₁ 245–50°. ³

(1,2-C₆H₄O₂(P(O₂C₆H₄)₂)₂. II. Plates, dec. 200°. ³

(*l*-Menthyl-oxy)-bis-(4-methyl-1,2-dioxiphenylene)phosphorus. II. Crystals, m. 65–70°. ⁶

COMPOUNDS HAVING DIRECT CARBON-PHOSPHORUS BONDS

(PhO)₃MePI. III. Needles, m. 75°. ²⁰**(PhO)₃EtPI.** III. Liquid. ²⁰**(PhO)₃(PhCH₂)PCI.** III. Liquid. ²⁰**(4-ClC₆H₄O)₃MePI.** III. Crystals, m. 71°. ²⁰**(3-MeC₆H₄O)₃MePI.** III. Hygroscopic powder. ^{8, 20}**(4-MeC₆H₄O)₃MePI.** III. Liquid. ^{8, 20}**Tri(trimethylphenoxy)-methylphosphorus iodide.** III. Liquid. The location of the methyl groups is uncertain. ²⁰**(PhO)₂(PhCH₂)PhPCI.** III. Needles, m. 193°. ^{16, 22}**(PhO)₂(PhCH₂)(4-MeC₆H₄)PCI.** III. Liquid. ¹⁶**(PhO)Ph₂MePI.** III. Needles, m. 134-6°. ²²**(PhO)(PhCH₂)Ph₂PCI.** III. Liquid. Decomposes at 232°. ²²

The following compounds may be either hydrogen-bonded adducts or true quasi-phosphonium compounds, Ph₃(ArO)POH. All were obtained by heating triphenylphosphine with the corresponding phenols. ¹⁰

Ph₃(2-MeC₆H₄O)POH. Crystals, m. 89-90°.Ph₃(3-MeC₆H₄O)POH. Crystals, m. 67°.Ph₃(4-MeC₆H₄O)POH. Crystals, m. 44-5°.Ph₃(2-ClC₆H₄O)POH. Crystals, m. 105-6°.Ph₃(4-ClC₆H₄O)POH. Crystals, m. 80-1°.Ph₃(2,6-Cl₂C₆H₃O)POH. Crystals, m. 97-8°.Ph₃(4-EtO₂CC₆H₄O)POH. Crystals, m. 104-5°.Ph₃(4-O₂NC₆H₄O)POH. Crystals, m. 107-8°.Ph₃(4-OHCC₆H₄O)POH. Crystals, m. 66-7°.Ph₃(PhO)POH. Crystals, m. 106°.**(N)-TYPE****(PhNH)₄P-** . IV. ^{9, 11} V. ¹⁴Chloride: prisms, m. 275°. ^{9, 11}Acetate: crystals, m. 206-7°. ¹⁴Propionate: crystals, m. 240°. ¹⁴Sulfate: crystals, m. 312-3°. ¹¹ Heating with strong sulfuric acid yields a water-soluble tetrasulfonate. ⁹

In the preparation of the chloride (V) it is possible to obtain small amounts of a poorly soluble substance, which has the composition (PhNH)₇P₂Cl, m. 192-4°; the true constitution of this material is uncertain. ⁹

(PhCH₂NH)₄PCI. IV. Plates, m. 208° (from EtOH). ¹⁷**2-MeC₆H₄NH)₄P-** . IV. ¹³Chloride: needles, dec. 254°. ¹³Nitrate: needles, m. 250°. ¹³Acetate: crystals, m. 221°. ¹⁴Chloroacetate: crystals. ¹⁴Propionate: crystals, m. 203°. ¹⁴Ethoxide: crystals, m. 114°. ¹³**(3-MeC₆H₄NH)₄PCI.** IV. Crystals. ⁹**(4-MeC₆H₄NH)₄PCI.** IV. Crystals. ⁹

(2,4-Me₂C₆H₃NH)₄P- . IV.¹³Chloride: crystals, dec. 264°. ¹³Nitrate: crystals, dec. 246-8°. ¹³Acetate: crystals, m. 210°. ¹⁴Methoxide: crystals, m. 98°. ¹²Ethoxide: crystals, m. 107°. ¹²

COMPOUNDS WITH DIRECT PHOSPHORUS-CARBON BONDS

(PhNH)₃PhP- . IV.²¹Chloride: needles, dec. 250°. ²¹Bromide: needles, m. 235°. ²¹Iodide: needles, m. 165°. ²¹Nitrate: crystals, m. 160°. ²¹Hydroxide: crystals, m. 216°. ²¹**(PhNH)₃(4-MeC₆H₄)P- . IV.²¹**Chloride: needles, m. 245°. ²¹Bromide: crystals, m. 238°. ²¹Iodide: crystals, m. 235°. ²¹Nitrate: crystals, m. 180°. ²¹Hydroxide: crystals, m. 240°. ²¹**(PhNH)₃(2,4,5-Me₃C₆H₂)P- . IV.¹⁵**Chloride: plates, m. 247°. ¹⁵Bromide: crystals, m. 259°. ¹⁵Iodide: crystals, m. 220°. ¹⁵Nitrate: crystals, m. 224°. ¹⁵Hydroxide: crystals, m. 203.5°. ¹⁵**(iso-Bu₂N)₂MePI₂. VI (from (R₂N)₂POPh and methyl iodide). Needles, m. 132°. ¹⁷****(C₆H₁₀N)₃MeP- . VI.²³**Iodide: crystals, m. 251-5°. ²³Hydroxide: hygroscopic alkaline mass. ²³**(C₆H₁₀N)₃EtPI. VI. Crystals, m. 178-9°. ²³****(C₆H₁₀N)₃-iso-BuPI. VI. Crystals, m. 172°. ²³****(C₆H₁₀N)₃(PhCH₂)PCI. VI. Hygroscopic mass. ²³****(C₆H₁₀N)₃MeP- . VI ¹⁸ (from phosphorus tri-tetrahydroquinolide).**Iodide: needles, m. 188°; chloroplatinate, m. 230°. ¹⁸Chloride: needles, m. 148-50°. ¹⁸**(C₆H₁₀N)₂MePhP- . VI.^{18, 24}**Chloride: needles, m. 130°; chloroplatinate, m. 178°. ^{18, 24}Bromide: needles, m. 97°. ^{18, 24}Iodide: plates, m. 167°. ²⁴Hydroxide: hygroscopic mass. ^{18, 24}**(C₆H₁₀N)₂EtPhI. VI. Needles, m. 174°. ^{18, 24}****(C₆H₁₀N)₂(PhCH₂)PhPCI. VI. Isolated as chloroplatinate, m. 204°. ^{18, 24}****(C₆H₁₀N)₂(4-MeC₆H₄)MeP- . VI.¹⁹**Iodide: crystals, m. 186°. ¹⁹Hydroxide: hygroscopic mass. ¹⁹**(C₆H₁₀N)₂(4-MeC₆H₄)EtPI. VI. Crystals, m. 191°. ¹⁹****(C₆H₁₀N)₂(4-MeC₆H₄)PrPI. VI. Crystals, m. 197°. ¹⁹****(C₆H₁₀N)₂(4-MeC₆H₄)-iso-BuPI. VI. Crystals, m. 204°. ¹⁹**

$(C_5H_{10}N)_2(4-MeC_6H_4)(PhCH_2)PI$. VI. Crystals, m. 125° .¹⁹
 $(C_9H_{10}N)_3MeP-$.

Iodide: needles, m. 188° .^{18, 23}

Chloride: crystals, m. $148-50^\circ$; chloroplatinate, m. 230° .¹⁸

$(C_9H_{10}N)_2MePhPI$. VI. Needles, m. 136° .¹⁸

COMPOUNDS OF PROBABLE QUASI-PHOSPHONIUM STRUCTURE

Me_2NPCI_4 . IV. Adduct with PCl_5 , dec. $242-4^\circ$.¹⁷

Et_2NPCI_4 . IV. Adduct with PCl_5 , dec. $232-3^\circ$.¹⁷

Pr_2NPCI_4 . VII. Crystals. IV. Adduct with PCl_5 , dec. 220° .¹⁷

$iso-Bu_2NPCI_4$. VII. Crystals. IV. Adduct with PCl_5 , dec. 168° .¹⁷

$MePhNPCI_4$. VII. Crystals.¹⁷

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Derivatives of Anhydro Acids

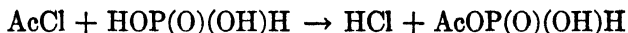
The substances considered in this chapter are, essentially, anhydrides of the various organic derivatives of phosphorus acids. This is probably the least-known branch of organic chemistry of phosphorus. At the very least, it is burdened with more confusing and contradictory information, carried from the past, than any other division of this subject. Only in the most recent years have even a few subdivisions of this general family of substances been clarified somewhat. This has been done in the realm of the pyrophosphate esters to a considerable extent because of the practical utility of the substances in this category in the insecticidal field.

METHODS OF PREPARATION

I. Direct acylation of phosphorus acids

Reactions of this type have been used for the synthesis of acyl phosphates and acyl phosphites, that is, mixed anhydrides. Few examples of individual reaction products are available.

Phosphorous acid is acetylated readily by acetyl chloride in acetic anhydride solution at 50°. ³¹ The product is isolated by careful filtration under anhydrous conditions.



Warming phosphorous acid with acetic anhydride has been reported to yield a similar product. ³² The extremely hygroscopic nature of such substances has precluded any true purification procedures.

Although the preparation of acetyl pyrophosphite was claimed some years ago in the course of heating phosphorous acid with phosphorus trichloride to 120°, ³³ there is no evidence that such a substance was truly isolated. Similarly, a reported preparation of a form of acetyl pyrophosphite by heating acetic acid with phosphorus trichloride is very doubtful. ³⁵ The product was isolated in the form of metal salts after extensive treatments in aqueous media, which should obviously hydrolyze any compound of the indicated structure.

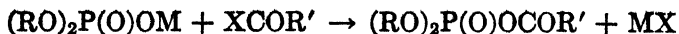
Acetylation of phosphoric acid by ketene, however, is an authentic and useful method for a simple synthesis of acetyl phosphoric acid.²⁸ The earlier observations of absorption of ketene by this acid were recently translated into the following synthetic method.^{28, 44} (Bentley.)

Ketene is passed, with good cooling, into 85% phosphoric acid in ether, and the resulting mixture is hydrolyzed with ice water. The removal of phosphate ion by barium hydroxide and the conversion of the soluble barium acetyl phosphate into the silver salt completes the process. The free acid may be obtained from the silver salt by means of hydrogen sulfide treatment. Partial esters of phosphoric acid may be used, and dibenzyl acetyl phosphate was prepared similarly from dibenzyl phosphate. Removal of the benzyl groups by catalytic hydrogenation also yields acetyl phosphoric acid.



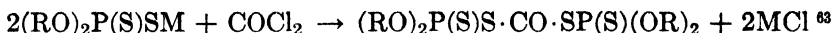
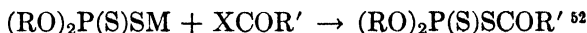
II. Reaction of metal salts of phosphorus acids with acid halides

Silver salts of phosphorus acids have found many applications in syntheses of this type. Thus trisilver phosphate reacts with an excess of acetyl chloride in cold ether to form triacetyl phosphate.⁵¹ The use of monosilver phosphate (prepared by trituration of the trisilver salt with phosphoric acid in ether) in a similar reaction was used to prepare the monoacetyl derivative, as well as a number of other acyl phosphates from the corresponding acyl chlorides.^{37, 49, 50} The products are isolated in the form of silver salts, although the higher members may be obtained in solid crystalline forms of the free acids. A convenient removal of the attendant phosphate ion is accomplished by freezing out in the form of trisodium phosphate.⁵⁰ The reaction may be regarded as coupling after cleavage of the elements of silver chloride. The use of trisilver phosphate, obviously, is capable of yielding all substitution products. Besides preparation by the use of the monosilver salt, indicated above, the monoacetyl derivative may be obtained by a "blocking" technique; silver dibenzyl phosphate is used, and the resulting dibenzyl acetyl phosphate is hydrogenated to remove the protective groups.⁵¹ The higher secondary esters of phosphoric acid may be used in such reactions in the form of the less expensive sodium salts; the stability of the higher acyl phosphates is sufficient to permit the use of the necessarily higher temperatures.⁸⁵ (Lynen; Lippman, Tuttle.)



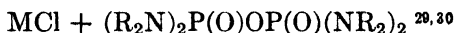
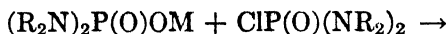
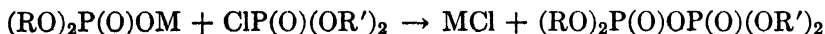
Reactions of this type have been described in the patent literature in connection with the synthesis of acyl derivatives of dithiophosphates.

Whereas the use of ordinary acyl halides yields the acyl derivatives as shown,



cyanogen chloride reportedly acts as a true halogen and yields a pyro derivative, $(RO)_2P(S)SP(S)(OR)_2$.⁵²

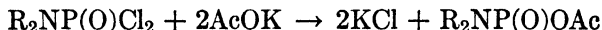
An extension of this reaction to the halides of phosphorus leads to a very useful synthesis of pyrophosphates and triphosphates. The basic reaction may be indicated as follows.



Although silver salts have been used in the research syntheses, obviously other salts may be used in this reaction, which is carried out in a suitable inert solvent. Usually the products are distilled for the necessary purification after filtration of the metal halide. Particularly interesting have been the applications of this reaction to the syntheses of biologically important nucleotides.^{23,24,78} If one of the groups R in the first equation is a benzyl group and both R' groups are likewise benzyl radicals, the reaction product is a tribenzyl pyrophosphate, which carries for its fourth ester group any desired radical; in the particular instance this radical is adenosine esterified in 5'-position. Debenzilation by hydrogen, using palladium oxide catalyst, converts the product smoothly into adenosine diphosphate (pyrophosphate).^{24,78} The starting material (silver 5'-adenosine benzyl phosphate) is readily obtained by partial hydrogenolysis of the dibenzyl ester, followed by conversion to the salt. The adenosine tribenzyl pyrophosphate, in turn, can be made to go through a similar cycle of reactions to be converted to the adenosine triphosphate (ATP).²³ The benzyl radical on the terminal phosphorus atom is preferably removed by hydrogen, and the resulting monohydrogen pyrophosphate ester is converted to the silver salt for this second operation. A somewhat smoother removal of the terminal benzyl group occurs when the neutral ester is warmed with N-methylmorpholine.²³ The result of the final coupling is adenosine tetrabenzyl triphosphate, which is readily hydrogenated to the free acid in which the arrangement of the three phosphorus atoms is definitely known.²³ (Todd *et al.*)

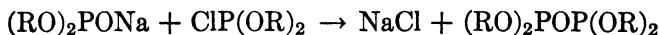
III. Reaction of halides of phosphorus acids with salts of organic acids

Reactions of this type have not been used extensively. As typical examples the reactions of dialkylamidodichlorophosphates or of the corresponding thiono derivatives with potassium acetate may be cited. The reactions are carried out conventionally by refluxing in inert solvents.^{29, 31} The reaction products are the corresponding acyl phosphates.

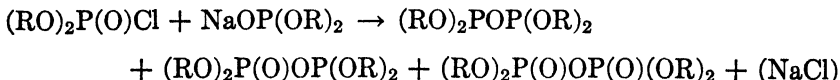


IV. Reaction of dialkyl sodium phosphites with halides of phosphorus acids

Although in principle the reaction of dialkyl phosphite salts with halophosphites or halophosphates may be expected to be a simple coupling reaction, actually it is considerably more complex and, as a rule, mixtures of various products are obtained. The most clean-cut reaction occurs between the above-mentioned salts (usually sodium derivatives are used) and dialkyl halophosphites. This reaction, carried out in inert solvents in the conventional manner, affords the best synthesis for tetra-alkyl pyrophosphites, which can be obtained only in very poor yields by other methods.^{13, 18, 20}



Reaction between sodium dialkyl phosphites and dialkyl chlorophosphates results in the formation of a mixture of tetra-alkyl pyrophosphites, hypophosphates, and pyrophosphates.^{14, 15, 18, 62, 66}



The origin of these products resides in the initial formation of dialkyl phosphite group, $(RO)_2PO$, which dimerizes to yield the hypophosphate and undergoes oxidation-reduction exchange to yield the other two products. As a rule, only small amounts of the pyrophosphite can be obtained, after careful fractionation, in pure state. The hypophosphate-pyrophosphate mixture can be resolved only after extensive fractionation, made difficult by the dissociative tendency of the pyrophosphate esters. However, oxidation of the crude mixture by oxygen at elevated temperatures may be resorted to for conversion of the products, in toto, to the pyrophosphate esters.⁶⁶ A modification of this reaction employs ethyl chlorosulfonate, $EtO \cdot SO_2Cl$, instead of the halophosphate. The expected product decomposes spontaneously and yields essentially the

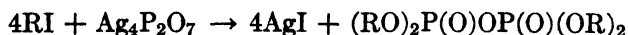
same mixture as above, in addition to trialkyl phosphate and sulfur dioxide. The trialkyl phosphate is formed from the alkoxyl ion and the dialkyl phosphite group, $(RO)_2PO$; the latter, of course, is the source of the other three esters.⁶⁸ The actual yields of individual products are rather low. (Nylén; Arbuzov.)

V. Reaction of halogens with dialkyl sodium phosphites

The reaction described in the previous section is essentially duplicated when the halophosphate is replaced by elemental halogens, chlorine or bromine. The reaction products are essentially the same as those obtained in the halophosphate reaction: tetra-alkyl pyrophosphites, hypophosphates, and pyrophosphates. Usually small amounts of dialkyl phosphite are found among the reaction products, as well as some trialkyl phosphate. When chlorine is the reagent, moderate amounts of dialkyl chlorophosphite may be isolated. The reaction employs one atomic equivalent of the halogen per mole of the sodium derivative, and the operation is performed in the cold, with adequate agitation. The principal reaction, again, is the formation of dialkyl phosphite ion, which is the source of the various products listed above. Usually petroleum ether is the solvent or diluent, although dry ether has been used. The yields of the individual esters are quite poor, and the separation requires extensive fractionation. It is interesting to note that this reaction was discovered in the course of investigation of the phosphorus-bearing component in the products of reaction between diethyl sodium phosphite and triarylmethyl bromides. The phosphorus is obtained in this case also in the form of dialkyl phosphite ion, which undergoes the same twinning and oxidation-reduction reactions as were represented above.^{14-8, 20} (Arbuzov.)

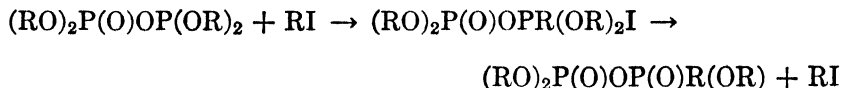
VI. Reaction of metal salts of phosphorus acids with alkyl halides

This classical method of ester formation has been used for the synthesis of tetra-alkyl pyrophosphates from tetrasilver pyrophosphate and the requisite alkyl iodides.^{36, 38, 42, 66, 72} The alkyl metaphosphates were also prepared similarly from either silver metaphosphate⁴⁷ or the lead salt.³⁴ The reactions are carried out by the conventional heating of the components, followed by separation of metal halide. Thus the pyrophosphate synthesis is shown below. (Cavalier; Clermont.)



However, the reported syntheses of tetra-alkyl hypophosphates or pyrophosphites using this method are erroneous.^{71, 72, 73, 75} Not only are

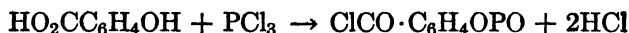
such esters capable of forming stable adducts with the silver halide from which it is impossible to isolate the esters proper, but all such esters, based on actual or potential trivalency of phosphorus, react with the alkyl iodides in the Michaelis-Arbuzov isomerization reaction so that the crude products are pyro derivatives of phosphonic acids. Thus the over-all reaction of this type may be shown as follows.



The extended studies made by the Arbuzovs showed that the alleged hypophosphates claimed by the earlier workers were indeed materials of this type, admixed to the silver halide adducts.¹⁶⁻⁸

VII. Reaction of salicylic acid derivatives with phosphorus trichloride

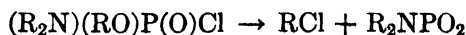
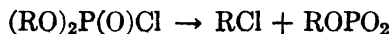
When salicylic acid (or substituted salicylic acid) is heated in boiling xylene with an excess of phosphorus trichloride, the carboxyl group of the acid is converted to the chloroformyl group whereas the phenolic group reacts with the trichloride to form a metaphosphite group, R—O—PO. It is probable that some form of intermolecular reaction between the primary products is responsible for the emergence of this unusual final structure.^{2,4,5,7-10} (Anschütz *et al.*)



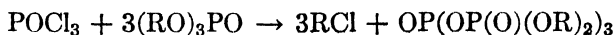
The products are isolated, in good yield, by distillation of the reaction mixtures after hydrogen chloride evolution subsides. The operations with these substances must be done under dry conditions.

VIII. Thermal decomposition reactions

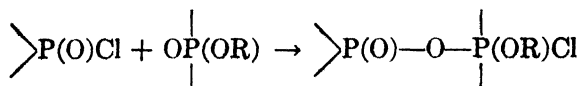
VIIIA. Reactions of halophosphates. The basic principle of this reaction, which yields various polyphosphate esters as the end products, consists of the elimination of alkyl halide from reaction mixtures in which substances with halophosphate groups and with phosphate ester groups are present. A rough representation of such reactions is given by the thermal decomposition of dialkyl chlorophosphates into alkyl chloride and alkyl metaphosphate,²⁷ the formation of tetra-alkyl pyrophosphates from phosphorus oxychloride or dialkyl chlorophosphate and trialkyl phosphate,^{42,76} and the formation of dialkylamido-metaphosphates from thermal decomposition of alkyl dialkylamido-chlorophosphates.^{20,30,58} (Michaelis; Schrader.)



Although the final products can be accounted for rather well in the simple cases shown above by the process of cleavage or displacement of the elements of alkyl halide, followed by juncture of the residuals, it appears very probable that the course of the reaction is not quite so simple as that. In all cases appreciable amounts of by-products are formed, by-products that are usually named metaphosphates or "decomposition" products. The reaction of phosphorus oxychloride with trialkyl phosphates is a good example of the more complex case. The original disclosure of this reaction indicated a triple loss of alkyl chloride, in the manner indicated above, resulting in the formation of a "hexa-alkyl tetraphosphate," presumably a tetraphosphate ester formulated on a pyramidal arrangement of three dialkyl phosphate groups around the phosphoryl group.⁷⁶



Subsequent investigations of the products of such reactions,^{42, 45} carried out recently, suggest that the final product is not an entity but a mixture that contains, among other substances, some tetra-alkyl pyrophosphates. The nature of the residual materials may be explained on the basis of the behavior of these substances on mild hydrolysis and on the basis of the known facts about phosphate esters in general.⁴⁵ It was shown some years ago that replacement of chlorine atoms in phosphorus oxychloride by ester groups greatly enhances the additive reactions of the phosphoryl group, reactions such as hydrogen bonding.²² It may be safely assumed that all the reactions discussed in this group may proceed by a mechanism that involves such addition. Thus ionization of the phosphorus to chlorine bond in the chlorophosphate structure should lead to addition of the resulting ions to the phosphoryl group of a molecule having a greater additive affinity; such additive affinity is shown by the phosphate esters. The result of such addition in general terms should form a quasi-phosphonium structure involving the formation of a pyrophosphate structure between the two molecules:

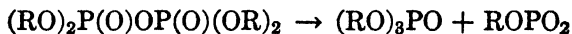


The resulting product may decompose by the usual loss of alkyl halide, characteristic of phosphonium halides, or the reaction may pro-

ceed to involve other molecules of the ester type, the driving force in each case being the difference of additive affinity. Although dialkyl chlorophosphate mixtures with trialkyl phosphates may be expected to terminate the reaction after one transfer of halogen, as shown above, it has been shown that the yields are not nearly quantitative and that the residuals in such reactions are similar to the residuals of reaction mixtures in which phosphorus oxychloride is used. These residuals are readily explained by the continuation of the chlorine donation, shown above, to form linear or cyclic chains of links of pyrophosphate type, with the possibility of termination at each added link by alkyl halide evolution. The most probable final products in such cases are cyclic structures in which three or four phosphorus atoms are bound by oxygen atoms, with the residual phosphorus valences occupied by alkoxy groups or semipolar oxygen linkages.⁴⁵ This formulation of the reaction mechanism gives an explanation of the appearance of both the linear pyrophosphates and the apparently "heterogeneous" residuals in these reactions. It is possible that the "hexa-alkyl tetraphosphate" may be a reality, but not in the sense of a pyramidal structure originally assigned to it. The cyclic polyphosphates of this type may be expected to be susceptible to hydrolytic attack, much in the manner actually observed. The cyclization mentioned above is a rather common event in phosphorus chemistry.

In practice such reactions are carried out by heating the reactants to a temperature in the vicinity of 150°. It is of interest to note that somewhat higher temperatures favor the formation of the pyrophosphates; this, again, is in line with the expectations of the mechanism given above. The decomposition of the primary quasi-phosphonium compounds may be expected to be facilitated by higher temperatures, while the chain continuation is made less favorable.

VIIIB. Thermal decomposition of polyphosphates. Although there is little doubt that many useful reactions may be found in this classification, only one such reaction has been subjected to fairly careful scrutiny. It has been shown that tetra-alkyl pyrophosphates are decomposed or dissociated on heating into trialkyl phosphates and alkyl metaphosphates.²⁷ (Balarew.)

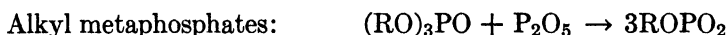
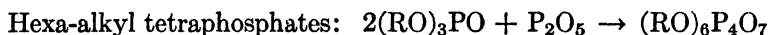
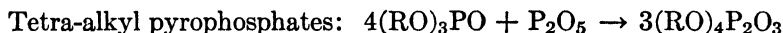


The reaction is believed to be reversible, and claims have been made concerning the preparation of the pyrophosphates by the reverse reaction. No definite evidence has been presented to support this view. The dissociation temperatures necessary for the foregoing reaction vary with the size of the alkyl groups. Ethyl derivative dissociates rapidly

at 200° or somewhat above, whereas the methyl compound is cleaved at 130°. ²⁷ Usually the resulting metaphosphate decomposes at such temperatures and yields olefin and metaphosphoric acid. ^{26, 27} The reaction, which obviously occurs with considerable disproportionation of the ester groups, may be used as a source of trialkyl phosphates from crude pyrophosphate or metaphosphate esters (see Chapter 9).

IX. Reaction of trialkyl phosphates with phosphorus pentoxide and of trialkyl tetrathiophosphates with phosphorus pentasulfide

Phosphorus pentoxide reacts readily with trialkyl phosphates to form complex esters of the condensed phosphoric acids. The reaction, per se, does not produce individual substances directly, and mixtures of the possible products may be expected. Theoretical equations given below may be used as guide for the formulation of reaction mixtures, which yield crude products of the general types shown. ¹ (Adler, Woodstock.)



The reaction is conducted by simple warming of the mixtures until a complete solution of the pentoxide takes place. The thermal instability of the higher esters limits this reaction to the lower esters. None of the products can be distilled, a fact that underlines their non-homogeneity. The mechanism of the reaction is unknown, but it must involve an attack not on the simple P_2O_5 structure but rather on the well-known complex network of oxygen-phosphorus bonds that represents the pentoxide in the solid state.

A similar reaction in the sulfur series has been reported. Heating trialkyl tetrathiophosphates, $(\text{RS})_3\text{PS}$, with phosphorus pentasulfide in the proportions indicated in the last equation results in the formation of the corresponding alkyl trithiometaphosphates, RSPS_2 . The reaction is conducted in hot xylene. ⁷⁴

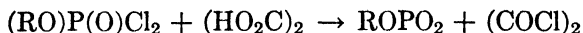
X. Reaction of ethers with phosphorus pentoxide

Heating dialkyl ethers (principally diethyl ether) with phosphorus pentoxide for several hours yields alkyl metaphosphates. The original description of the reaction, given by Langheld, ^{46, 47, 69} was later shown to be unworkable, and the current procedure involves such heating,

preferably with agitation, in the presence of a halogenated hydrocarbon, usually chloroform.⁷⁷ The clear solution obtained after several hours is diluted with dry ether, which results in precipitation of the metaphosphate in the form of a heavy oil. This procedure has been used only for the ethyl ester and may be unsuitable for the higher esters that have modified solubility characteristics. The products cannot be distilled. Diphenyl ether does not react; dibenzyl ether merely forms polymers.⁸⁸ The mechanism of the reaction has not been investigated, but it probably has points of similarity with the reactions given in Sections VIII and IX. (Langheld.)

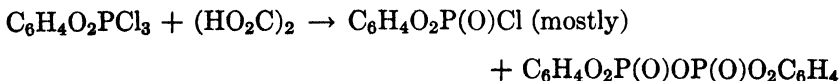
XI. Reaction of dichlorophosphates with oxalic acid

Heating dichlorophosphates, preferably of the aryl series, with equimolar amounts of dry oxalic acid to 75 to 85° forms the corresponding metaphosphates.^{3, 6, 10, 39}



The reaction has found its widest application among the derivatives of salicylic acid, studied extensively by Anschütz. In particular, it has been applied to the chloroformylphenyl dichlorophosphates; the metaphosphate derivatives of this type may be purified by distillation.

A similar reaction of catechylphosphorus trichloride yields much *o*-phenylene chlorophosphate, by the usually expected exchange of two chlorine atoms for the semipolar oxygen, but some di-*o*-phenylene pyrophosphate is also formed.¹³ The formation of this product is not clearly understood.



XII. Reaction of phosphonyl dichloride with phosphonic acids

Phosphonyl dichlorides react smoothly with the corresponding primary phosphonic acids on heating, usually in benzene solution, with elimination of hydrogen chloride and the resultant formation of metaphosphonates. The products are isolated by crystallization under anhydrous conditions.^{41, 56, 57, 59, 60}



These products may be obtained by heating phosphonic acids with phosphorus pentachloride, taken in appropriate proportion in order to convert one half of the free acid into the phosphonyl dichloride. Usually this variation of the method gives less pure products. (Michaelis.)

XIII. Partial hydrolysis of higher polyphosphates

Although it is logical to believe that careful hydrolysis or alcoholysis of esters (or amides) of highly condensed phosphoric acids should give products of a lower order of condensation (or dehydration), not a single instance of isolation of any definite individual substance by methods of this type has been reported. This is true in part because esters of acids higher in order than the pyrophosphates have not been isolated in individual states.

Procedures of this type, however, are used to destroy the higher orders of phosphates in crude reaction mixtures obtained by methods given in Sections VIII and IX. This destruction permits the isolation, by distillation route, of the pyrophosphate esters obtained in the reaction. The procedure used depends upon relatively rapid hydrolysis of such higher phosphates in comparison with the pyro esters, and actually consists of a rapid washing of the crude mixture with cold water, followed by the extraction of the pyrophosphates (neutral esters) with an organic solvent such as benzene or chloroform.^{42,79} Unless the higher esters are removed, distillation of the pyrophosphates as prepared by the methods indicated above is essentially impossible because of the thermal decomposition of the crude mixtures. Such treatment is particularly important for the isolation of tetra-alkyl pyrophosphates from reaction mixtures obtained by modifications of the procedure of Section VIIIA, in which alcohols and phosphorus oxychloride are permitted to react in a sequence of reactions simulating the reaction of trialkyl phosphate with dialkylchlorophosphate. Such conditions are obtained when the molar ratio of the reactants is nine to four, respectively.⁸⁰ (Hall; Toy.)

XIV. Controlled hydrolysis of secondary chlorophosphates

Reactions of this type are basically similar to the reactions of halophosphates with salts of phosphate esters (see Section II). The secondary chlorophosphates are permitted to react with a limited amount of water in the presence of a theoretical amount of a base (pyridine is usually preferred, although sodium bicarbonate may be used) to take up the hydrogen chloride. Although solvents such as ether may be used, they are not essential. However, temperatures should be moderate to prevent further degradation of the products. In effect, the reaction is a two-step process consisting of the hydrolysis of part of the chlorophosphate to the free acid ester and of the reaction of the ester in the presence of the base with the residual chlorophosphate. Although the base may be omitted and the hydrogen chloride removed by evacuation of the mixture, the yields of the pyrophosphates are reduced.⁷⁹



The higher esters, such as the benzyl derivative, may be used in this reaction with even stronger bases, such as aqueous potassium hydroxide.⁴⁰ Instead of the secondary chlorophosphates per se, the reaction of secondary phosphites with aliphatic polyhalides in the presence of bases may be used. This reaction probably yields the corresponding secondary halophosphates (see Chapters 8, 9, and 10). The products undergo the hydrolytic coupling as described above under proper conditions. Thus tetrabenzyl pyrophosphate is readily prepared from dibenzyl phosphite, carbon tetrachloride, and aqueous potassium hydroxide at room temperature.²¹

As was mentioned in Chapter 9, the higher primary and secondary esters of phosphoric acid frequently display properties analogous to those expected of the pyrophosphates, such as lack of titratable hydrogen in the secondary esters or a deficiency of one in the primary esters. Whether or not these properties are caused by the formation of true pyrophosphates, the fact remains that so far as the ordinary chemical behavior is concerned such esters are very similar to the pyro esters. Examples of this type arise when aryl hydroxy compounds or very large aliphatic or aralkyl hydroxy derivatives are permitted to react with phosphorus oxyhalides in proportions designed for the formation of halophosphates and the reaction mixtures are treated with aqueous bases. The products obtained are substances of this type.^{61, 64, 65} It is unfortunate that no information is on hand to delineate the scope of this modification. (Deutsch, Ferno; Todd *et al.*; Toy.)

XV. Reaction of hydroxy compounds with derivatives of anhydrophosphoric acids

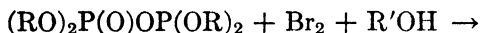
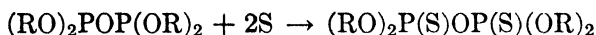
Although the patent literature contains references to the formation of esters of the phosphoric acids of the higher orders of condensation by reaction of alcohols with partial esters of such acids, the reactions of this type may be expected to be alcoholytic in character and to produce esters of phosphorus acids of lower orders, since the most rapid action of esterification takes place in the progressive cleavage of phosphorus to oxygen to phosphorus bonds between the units of phosphoric acid present in such esters. No specific substances have been isolated in procedures of this type. Similarly, attempts to form esters of pyrophosphoric acid from alcohols and pyrophosphoryl chloride failed.⁸⁴

However, it has been shown that, although pyrophosphoric acid and its acid salts do not form pyrophosphate esters with alcohols, acid pyrophosphate esters are produced in fair yields when metaphosphoric acid

is heated with the hydroxy compounds.^{86,87} Pyrophosphates of thiamine and related compounds were obtained upon heating these substances with metaphosphoric acid to 150°. Usually a little sodium pyrophosphate added to the mixture has a favorable effect on the yields. The meta acid may be obtained either by partial hydration of phosphorus pentoxide or, in the crude state, mixed with pyrophosphoric acid, by solution of the pentoxide in pyrophosphoric acid, or by dehydration of sirupy acid.⁸⁷

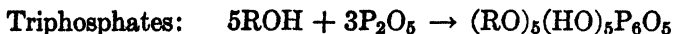
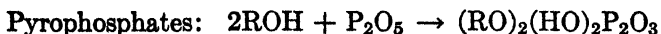
XVI. Addition of sulfur or oxygen to trivalent derivatives

The reactions considered here are not used to establish the structures of the condensed acid types but rather to modify the already formed molecules. Thus tetra-alkyl pyrophosphites or hypophosphates have the ability to add two or one atoms of oxygen or sulfur, respectively, to form the tetra-alkyl thionopyrophosphates. This behavior suggests the presence of two trivalent phosphorus atoms in the first class and of one in the second class. The addition of sulfur is done conventionally by warming in an inert solvent. Oxidation may be performed by oxygen stream with heating or by treatment with bromine followed by alcoholysis of the dibromo derivative formed at each trivalent phosphorus atom. Thus the general reaction type may be shown as follows.^{16-8, 66}



XVII. Reaction of alcohols with phosphorus pentoxide and of thiols with phosphorus pentasulfide

Although crude mixtures of partial esters of phosphoric acids of the higher orders of condensation are obtained upon reaction of the alcohols with phosphorus pentoxide, individuals have not been isolated from such mixtures. The reaction, which is considered in more detail in Chapter 9, is a progressive attack of ROH upon the network of phosphorus to oxygen bonds that composes the complex units of the anhydride. As such, it cannot produce clean-cut individual products until the final stage of alcoholysis is reached and only the esters of phosphoric acid are left. However, crude and approximate mixtures may be formulated in accordance with the following expressions.¹



The reaction of thiols with phosphorus pentasulfide is similar, but there is little information about the products obtainable. It has been shown that the reaction of aromatic thiols with the pentasulfide conducted in boiling toluene with a four-to-one molar ratio yields primarily the aryl trithiometaphosphates, $RSPS_2$.⁷⁴ Some tetrathiophosphate, $(RS)_3PS$, usually may be found among the by-products. The meta derivatives are insoluble in organic solvents and are readily separated.



The products must be handled under anhydrous conditions to prevent hydrolysis.

GENERAL CHARACTERISTICS

All the substances discussed in this chapter are essentially acid anhydrides. As such they are subject to attack by hydrolytic or alcoholic means, which progressively converts them to compounds of the lesser order of complexity. Thus the pyrophosphates, which have received most of the attention, are smoothly hydrolyzed to the component phosphates. The metaphosphates, however, do not hydrolyze or alcoholize in the above manner under moderate conditions. Considerable disproportionation occurs and a spectrum of phosphates is usually produced. The aryl trithiometaphosphates, however, react rather smoothly with thiols and form the corresponding tertiary tetrathiophosphates,⁷⁴ although hydroxy compounds react by displacement of the thioaryl groups and form secondary dithiophosphates and thiols.⁷⁴

Only the lower esters of pyrophosphoric, pyrophosphorous, and hypophosphoric acids are distillable. The other derivatives decompose on attempted distillation.

It is interesting to note that acyl phosphates are capable of acylation reactions upon treatment with amines; no phosphorylation, however, takes place.²⁸ The pyrophosphates display phosphorylation reactions with primary amines, well expressed by tetrabenzyl pyrophosphate.²¹ The tetra-alkyl hypophosphates react with primary amines, but the products are not dialkyl amidophosphates. They are instead acidic substances or, at least, substances that display acidic properties upon treatment with water; the second product of the reaction is dialkyl phosphite.¹⁹ Reinvestigation of original claims of phosphorylation of amines by alkyl metaphosphates showed that they are unfounded.^{46-48, 70}

Tetra-alkyl pyrophosphites are typical trivalent phosphorus esters and, as such, add two molecules of metallic halides, enter the isomerization reactions with alkyl halides, and are very readily attacked by

hydrolysis. There is little doubt that they can be formulated as $(\text{RO})\text{POP}(\text{OR})$.

Tetra-alkyl hypophosphates behave in a manner suggestive of one trivalent phosphorus atom in their constitution, as shown by the reactions of the types listed above. However, it is possible to regard them as dimers of the dialkyl phosphite ion, $(\text{RO})_2\text{PO}$. Certainly the reactions used in the preparation of these esters proceed by the way of formation of such bodies and their twinning is to be expected. The precise manner of such twinning, however, is not quite clear, and although much of the purely chemical evidence, such as that produced by Arbuzov,¹⁶⁻⁸ seems to support the unsymmetric structure $(\text{RO})_2\text{P}(\text{O})\text{OP}(\text{OR})_2$, other formulations cannot be completely excluded at this time.^{62, 67} It is interesting to note that alcoholysis of such esters produces four products, dialkyl phosphate and trialkyl phosphite, as well as trialkyl phosphate and dialkyl phosphite. The latter pair is formed in approximately one-third the yield of the first pair. Formulation of these results on the basis of the unsymmetric structure given above signifies that the expected quasi-phosphonium primary adduct of the alcohol, $(\text{RO})_3\text{P}(\text{OH})\text{OP}(\text{OR})_2$, decomposes primarily in one direction. Investigation of the reactions of such esters may be expected to shed much light on the reaction mechanisms of phosphorus compounds in general, a subject about which little is known at the present time.

The pyrophosphates may be represented quite certainly by the symmetric representation $(\text{RO})_2\text{P}(\text{O})\text{OP}(\text{O})(\text{OR})_2$. For esters that contain sulfur atoms as well as oxygen atoms, such as are formed in the sulfurization of pyrophosphites and hypophosphates, the picture is not clear. Although the thiono structure is given in the appended list of compounds, the possibility of a shift to phosphorus to sulfur to phosphorus structure is not unreasonable in view of the known displacement of sulfur from semipolar attachment to phosphorus by oxygen.

The alkyl metaphosphates present a structural problem somewhat similar to that of the hypophosphates. The principal difference in the monomer structures of these units lies in the presence of the semipolar oxygen in place of an electron pair at the phosphorus atom. In the free state the metaphosphate esters are highly associated; thus cryoscopic data indicate a hexamer aggregation.⁶⁹ Such structures may be expected to be cyclic, at least in part, and the formation of six-membered rings composed of three phosphorus atoms and three oxygen units is rather likely. Molecular weight determinations in boiling solvents indicate lower aggregations, such as dimers. At any rate, the usual presentation of such esters as ROPO_2 , especially with two double-

bonded oxygen atoms, is quite inadequate or even erroneous so far as the explanation of the reactions of these substances is concerned. Their formation from ethers and phosphorus pentoxide, which definitely has a highly condensed cyclic structure, is suggestive of the normally cyclic nature of the esters themselves. The metaphosphonates are most probably constituted along the similar states of aggregation, as are the metaphosphates.

Recently the interest in the compounds of the pyrophosphate type has been turned into definitely practical channels. These substances, as a class, possess clearly defined action of anticholinesterase type. The most potent activity among the tetra-alkyl esters in this family appears in compounds with two or three carbon alkyl chains, and the more or less pure preparations of tetraethyl pyrophosphate have been rather widely used as potent insecticidal agents. The action of these substances on living matter appears to be similar to that of the fluorophosphates. In such applications the inherent toxicity to warm-blooded animals must be always kept in mind. The incipient toxic symptom is usually a sharp contraction of the eye pupil, analogous to that encountered after intoxication with dialkyl fluorophosphates. Continued exposure at high levels may terminate fatally even in man. It may be mentioned that the tetra-alkyldiamides of this series, $(R_2N)_2PO \cdot O \cdot PO(NR_2)_2$, appear to confer systemic insecticidal potency to plant tissues upon absorption. Although it would appear that the pyrophosphate link, per se, and its thio analogs are the essential bio-active structural units, it is quite impossible at this time to set the limits upon possible modifications of the remainder of the molecule that would largely preserve the biological activity and reduce the rate of hydrolytic attack, which at this time is a major problem in practical use of these substances as insecticides.^{29, 30}

ACYL PHOSPHITES AND ACYL PHOSPHATES

- MeCO·OPO₂H₂.** I (using acetyl chloride).⁵¹ I (using acetic anhydride).⁵² Hygroscopic plates.⁵² dec. 100°. ⁵¹
- MeCO·OP(OH)·OPO₂H₂(?).** I (from acetyl chloride and phosphorous acid at 120°). Isolated as potassium, barium, and lead salts.⁵³ Sirup, forming a crystalline dihydrate. The structure is questionable.
- MeC(OH)(OPO₂H₂)₂(?).** I (from acetic acid and phosphorus trichloride, followed by heating to 120–30°).⁵⁵ Calcium salt claimed. The structure is questionable in view of the apparent stability to treatment in aqueous media.⁵⁵
- MeCO·OP(O)(OH)₂.** I (using ketene).⁵⁶ II (from "mono"silver phosphate),⁵⁰ (from silver dibenzyl phosphate).⁵¹ Silver salt, needles.^{53, 51} Lead salt, poorly soluble solid, needles.⁵¹ Free acid, sirup (from lead salt).⁵³ Half life at 38° at pH 7.4 is 3 hours.⁵¹

(MeCO·O)₃PO. II (from silver phosphate).⁵¹ Plates, m. 59–61° (from Et₂O).⁵¹

Very hygroscopic and readily hydrolyzed, probably to the diacetyl derivative, which readily passes on to phosphoric acid, as the hydrolysis rates of mono- and diacetyl derivatives appear to be nearly identical.⁵¹

MeCO·OP(O)(OH)OP(O)(OH)₂(?). XVI. Barium salt isolation is claimed: acetyl pyrophosphite (see above) is oxidized by BaO₃.⁵⁴ The slowness of reported hydrolysis by hot acids or bases makes this structure dubious.

EtCO·OP(O)(OH)₂. II (from "mono"silver phosphate). Silver salt.⁵⁰

PrCO·OP(O)(OH)₂. II (from "mono"silver phosphate). Silver salt.⁵⁰

C₇H₁₅CO·OP(O)(OH)₂. II (from "mono"silver phosphate). Silver salt, solid, by precipitation with silver nitrate from slightly acid solution. Sodium, barium, calcium, and strychnine salts prepared by metathesis. Half life at 37° and pH 7.4 is 12 hours.⁴⁹

C₁₅H₃₁CO·OP(O)(OH)₂. II (from "mono"silver phosphate).⁴⁹ Hygroscopic plates, dec. 61–3° (from benzene-ligroin). Metathesis was used to isolate the following poorly soluble salts: silver, calcium, barium, and strychnine (useful for the separation from inorganic matter). Half life is comparable to the C₈ derivative.

(HO₂C·CH₂CH₂CO)OP(O)(OH)₂. II (from "mono"silver phosphate) results in formation of both mono- (illustrated) and the diphosphate derivatives. Isolated as silver salts.⁵⁰

PhCO·OP(O)(OH)₂. II (from "mono"silver phosphate). Silver salt isolated. Half life at 37° and pH 7.4 is 4.5 hours.³⁷

(PhCO·O)₂P(O)OH. II (from silver phosphate). Sodium salt isolated. Half life at 37° and pH 7.4 is 45 hours.³⁷ One benzoyl group is readily available for N-benzoylations in water solution.³⁷

Cinnamoyl (S,S)-dicholesteryldithiophosphate. PhCH:CHCO·P(O)(SR)₂(?). II (from cinnamoyl chloride and the sodium salt).⁸⁵ Crystals, m. 153–5° (from CHCl₃).⁸⁵

(MeCO)₂P(OH)₃(?). This derivative of ortho structure is claimed to be produced by II (from silver phosphate).³⁵ It is probably crude triacetyl phosphate.

Me₂NP(O)(O·COMe)₂. III. Undistillable oil.⁸¹

Me₂NP(S)(O·COMe)₂. III. Undistillable oil.⁸¹

C₆H₁₀NP(O)(O·COMe)₂. III. Undistillable oil.⁸¹

ESTERS OF PYROPHOSPHOROUS ACID

(EtO)₂POP(OEt)₂. IV (best from diethyl chlorophosphite).¹⁸ V (using bromine or chlorine).^{15,16} Liquid, b₁₁ 102–4°,¹⁸ b₄ 87–8°,¹⁶ b₂₋₃ 82–3°,^{15,16} d₄⁰ 1.0748,¹⁸ n_D¹⁹ 1.4377,¹⁸ n_D²⁰ 1.4322;¹⁸ adducts: 2CuCl, m. 111.5–2.5°; 2CuBr, m. 135–6°; 2CuI, m. 119–21°; 2AgCl, dec. 115–6°.¹⁶

(PrO)₂POP(OPr)₂. IV (best from dipropyl chlorophosphite). V (using bromine).²⁰ Liquid, b₆ 147.5–49°, d₄⁰ 1.0664, n_D^{16,5} 1.4408.²⁰

(BuO)₂POP(OBu)₂. IV (from dibutyl chlorophosphite). Liquid, b₇ 175–6°, d₄¹⁵ 0.9908, n_D²⁰ 1.4451.¹³

ESTERS OF HYPOPHOSPHORIC ACID

As pointed out by Arbuzov, the reported preparations of methyl, ethyl, propyl, isobutyl, and benzyl esters by method VI,⁷¹⁻⁷⁵ are in error. Authentic preparations are:

- (EtO)₂P(O)OP(OEt)₂.** V (using bromine).^{14,16} Liquid, b_2 116–7°, d_4^0 1.1457, $d_4^{18.5}$ 1.1283, n_D^{20} 1.4284.¹⁶
- (PrO)₂P(O)OP(OPr)₂.** V (using bromine).²⁰ Liquid, $b_{3.5}$ 167–70°, d_6^0 1.1171, $n_D^{21.2}$ 1.4278.²⁰

ESTERS OF PYROPHOSPHORIC ACID AND ALLIED PRODUCTS

1. ESTERS OF PYROPHOSPHORIC ACID

- (MeO)₂P(O)OP(O)(OMe)₂.** VI.⁷⁸ IX.¹ XIV.⁷⁹ Liquid, $b_{0.5}$ 114–6°, d_4^{25} 1.3609, n_D^{25} 1.4121.⁷⁹
- (EtO)₂P(O)OP(O)(OEt)₂.** IV.⁶⁶ V.^{14,16,18} VI.^{36,38,42,66,72} VIIIA.⁴² VIIIB(?).²⁷ IX.¹ XIII.^{42,79} XIV (best, using pyridine).⁷⁹ Liquid, b_8 166–70°,⁶⁶ b_8 155–5.5°, b_8 144–5°,¹⁶ b_{1-2} 140°,⁶⁶ b_1 135–8°, $b_{0.5}$ 125–30°; ⁷⁹ best sample is said to have: $b_{0.08}$ 104–10°; ⁴² d_6^0 1.2040 ^{14,16}(?), d_4^{24} 1.1901,⁷⁹ d_4^{20} 1.172,⁶⁶ d_4^{17} 1.1978,⁷⁹ d_6^{20} 1.1847; ¹⁴ best sample is claimed to have n_D^{25} 1.4170; ⁴² and d_5^{25} 1.1845; ⁴² n_D^{20} 1.4222 (high ?),^{14,16} n_D^{25} 1.4182,⁷⁹ n_D^{20} 1.417.¹ Ethylene evolution begins at 208°. ⁴²
- (PrO)₂P(O)OP(O)(OH)₂(?).** Claimed to be formed from ethyl metaphosphate and propanol. Isolated as barium salt.⁷⁰
- (PrO)₂P(O)OP(O)(OPr)₂.** V.²⁰ VI.³⁶ XIV (using pyridine).⁷⁹ Liquid, b_4 178–9.5°, ²⁰ $b_{0.01}$ 112–6°, ⁷⁹ d_4^0 1.1211, ²⁰ d_4^{25} 1.1037,⁷⁹ $n_D^{17.5}$ 1.4300,²⁰ n_D^{25} 1.4248.⁷⁹
- (iso-PrO)₂P(O)OP(O)(OPr-iso)₂.** XIV (using pyridine).⁷⁹ Liquid, $b_{0.01-0.02}$ 92–5°, d_4^{25} 1.0854, n_D^{25} 1.4170.⁷⁹
- (BuO)₂P(O)OP(O)(OBu)₂.** VI.³⁶ IX.¹ XIV (using pyridine).⁷⁹ Liquid, $b_{0.01}$ 143–6°, d_4^{25} 1.0533, n_D^{25} 1.4296.⁷⁹
- (iso-AmO)₂P(O)OP(O)(OAm-iso)₂.** VI. Liquid.³⁶
- Dimethyl pyrophosphate.** (RO)₂P(O)OP(O)(OH)₂(?). XIV. Crystals, m. 198° (from EtOAc).⁶¹ Lead, silver, and calcium salts prepared.⁶¹
- (PhCH₂O)₂P(O)OP(O)(OCH₂Ph)₂.** XIV (either from dibenzyl chlorophosphate and cold potassium hydroxide solution, or from dibenzyl phosphite and potassium hydroxide in presence of CCl₄). Crystals, m. 60–1° (from Et₂O-cyclohexane),²¹ m. 59–60°. ⁴⁰
- (PhO)₂P(O)OP(O)(OH)₂(?).** XIV (from phenol and 1.4 moles of POCl₃ in pyridine). Potassium salt, needles (from dil. EtOH).⁶⁵
- HO(2-MeC₆H₄O)P(O)OP(O)(OC₆H₄Me-2)OH(?).** XIV (as above). Free acid: sirup. Potassium salt, needles (from EtOH).⁶⁴
- o-C₆H₄O₂P(O)OP(O)O₂C₆H₄.** XI (from RO₂PCl₃ and oxalic acid). Crystals, m. 136–8°, b_{12} 222°. ¹³
- Thiamine chloride pyrophosphate (cocarboxylase).** VI (from bromothiamine and silver pyrophosphate).⁸⁸ XV (from thiamine hydrochloride and metaphosphoric acid).⁸⁷ Crystals, m. 238–40° (from EtOH- 0.1 N HCl).^{88,87}
- 4-Methyl-5-thiazolyl-ethyl pyrophosphate.** XV (from dehydrated phosphoric acid at 150°). Trisilver salt, needles (from water).⁸⁷
- Adenosine-5'-pyrophosphate.** II (from dibenzyl chlorophosphate and the silver salt of adenosine-5'-phosphate monobenzyl ester, followed by hydrogenolysis). Barium salt, solid. Acridine salt, m. 215° (from water).³⁴

2. AMIDES OF PYROPHOSPHORIC ACID

- (Me₂N)(EtO)P(O)OP(O)(OEt)(NMMe₂).** VIIIA. Liquid, b_{13} 137°. ²⁰
- (Me₂N)(EtO)P(O)OP(O)(NMMe₂).** VIIIA. Liquid, b_8 145°. ²⁰

$(\text{Me}_2\text{N})_2\text{P}(\text{O})\text{OP}(\text{O})(\text{NMe}_2)_2$. II. VIIIA. Liquid, b_2 142°. ^{29,30}

$(\text{PhNH})_2\text{P}(\text{O})\text{OP}(\text{O})(\text{NHPH})_2$. II (from $(\text{PhNH})_2\text{POCl}$ and the corresponding acid in pyridine). XIV (using pyridine). Needles, m. 222°. ⁶⁰

3. ESTERS OF THIONO AND DITHIONO ACIDS

$(\text{EtO})_2\text{P}(\text{O})\text{OP}(\text{S})(\text{OEt})_2$. XVI (from the hypophosphate). Liquid, b_3 147.5–8.5°, d_4^{20} 1.2067, d_4^{20} 1.1887, n_D^{20} 1.4508. ¹⁶

$(\text{EtO})_2\text{P}(\text{S})\text{OP}(\text{S})(\text{OEt})_2$. Claimed to form in the action of concentrated sulfuric acid on $(\text{EtO})_3\text{PS}$. ^{23,34} XVI(?). ²⁹ Liquid, b_2 135°. ²⁹

$(\text{EtO})_2\text{P}(\text{S})\text{SP}(\text{S})(\text{OEt})_2(?)$. Claimed to form in heating $(\text{EtO})_3\text{P}_2\text{S}_3\text{Br}$ and ethanol, followed by aqueous treatment. Liquid. ⁵⁵

$(\text{EtO})_2\text{P}(\text{S})\text{SP}(\text{S})(\text{OEt})\text{Br}(?)$. Claimed to form in reaction of $\text{P}_2\text{S}_3\text{Br}_4$ with ethanol. Undistillable oil. ⁵⁵

$(\text{EtS})_2\text{P}(\text{S})\text{SP}(\text{S})(\text{SEt})_2(?)$. From $\text{P}_2\text{S}_3\text{Br}_4$ and aqueous ethanol. ⁵⁵ By action of sulfuric acid on triethyl dithiophosphate. ⁵⁵ Solid, m. 71.2°. The preparations should be checked.

ESTERS OF PYROPHOSPHONIC ACIDS

$\text{EtP}(\text{O})(\text{OEt})\text{OP}(\text{O})(\text{OEt})_2$. By reaction of ethyl iodide with tetraethyl hypophosphate. Liquid, b_3 147–7.5°, d_4^{20} 1.1808, d_4^{20} 1.1539, n_D^{20} 1.4280. ¹⁶

$\text{Ph}_3\text{CP}(\text{O})(\text{OMe})\text{OP}(\text{O})(\text{OMe})\text{CPh}_3$. VIIIA (from dimethyl triphenylmethane-phosphonate, on heating with PCl_5). As a by-product, in methylation of the free acid with dimethyl sulfate in the presence of potassium carbonate. Crystals, m. 227–33° (from $\text{CHCl}_3\text{-Et}_2\text{O}$). ⁴³

$\text{Ph}_3\text{CP}(\text{O})(\text{OEt})\text{OP}(\text{O})(\text{OEt})\text{CPh}_3$. VIIIA (as above). From the free acid (see above). Two crystalline forms: m. 222–3° and m. 228–31°. ⁴³ The free acid (by hydrolysis of either ester by means of AcOH-HI or dilute HCl at 200°), m. 267–70° (from benzene- Et_2O). ⁴³

$(4\text{-MeC}_6\text{H}_4)_2\text{P}(\text{S})\text{OP}(\text{S})(\text{C}_6\text{H}_4\text{Me-4})_2$. XIV (using water at 130°). Crystals, m. 165–6°. ⁶⁷

ESTERS OF TRIPHOSPHORIC ACID

The products obtained by procedure IX are probably not pure individuals. The only truly individual preparation is:

Adenosine-5'-triphosphate. ATP. II (repeated procedure used for the synthesis of the pyrophosphate analog). ²³ Barium salt and triacridine salt, m. 209°, isolated. ²³

ESTERS OF METAPHOSPHOROUS ACID

2-CICO·C₆H₄OPO. VII. Crystals, m. 36–7°, b_{11} 127°. ⁵

2-CICO-4-ClC₆H₃OPO. VII. Hygroscopic solid, m. 55–7°, b_{14} 155–6°. ⁴

2-CICO-6-ClC₆H₃OPO. VII. Crystals, m. 65°, $b_{12.5}$ 150°. ⁴

2-CICO-4,6-Cl₂C₆H₂OPO. VII. Crystals, m. 55–6°, b_{11} 159°. ⁷

2-CICO-4,6-Br₂C₆H₂OPO. VII. Crystals, m. 75–6°, b_{12} 210°. ⁸

2-CICO-4,6-I₂C₆H₂OPO. VII. Green-yellow solid, m. 126°. ⁹

2-CICO-4-MeC₆H₃OPO. VII. Crystals, m. 61°, b_{12} 145.6–6.4°. ¹⁰

2-ClCO-5-MeC₆H₃OPO. VII. Crystals, m. 45°, b₁₃ 150-1°. ¹⁰

2-ClCO-6-MeC₆H₃OPO. VII. Crystals, m. 36-7°, b₁₄ 143.6-4.0°. ¹¹

ESTERS OF METAPHOSPHORIC ACID AND ALLIED SUBSTANCES

1. ESTERS OF METAPHOSPHORIC ACID

(MeOPO₂)₂. VIIIA. ²⁷ VIIIB. ²⁷ IX. ¹

(EtOPO₂)₂. VI. ⁴⁷ VIII (special; by heating diethyl phosphate)(?). ⁴⁷ VIIIA. ²⁷ IX. ¹ X; ^{46, 47, 69} best procedure. ⁷⁷ Prepared by VI (from lead metaphosphate) ³⁴ the substance is said to be distillable: b. about 100° (?). Reliable data indicate the material to be undistillable. It is a sirupy fluid, soluble in halogenated solvents and insoluble in ether (usual purification method). The lack of good purification methods makes its constants uncertain; d₄²⁵ 1.42, n_D²⁵ 1.438 is probably a fair set of values. ¹ Freezing point method (in naphthalene) yields hexameric mol. wt.; boiling point (in CHCl₃) yields dimeric value. ^{69, 70}

(BuOPO₂)₂. IX. ¹ Unstable liquid, d₄²⁵ 1.227, n_D²⁵ 1.445. ¹

(C₈H₁₇OPO₂)₂. IX. Unstable at room temperature; d₄²⁵ 1.151, n_D²⁵ 1.45. ¹

2. CHLOROFORMYL ESTERS OF METAPHOSPHORIC ACID

2-ClCO·C₆H₄OPO₂. XI. VIIIA. ^{3, 39} Crystals, m. 95° (from benzene-ligroin), b₁₁ 170-1°. ^{3, 39}

2-ClCO-4-MeC₆H₃OPO₂. XI. Plates, m. 88° (from Et₂O), b₁₄ 185-6°. ¹⁰

2-ClCO-5-MeC₆H₃OPO₂. XI. Plates, m. 77° (from Et₂O), b₁₄ 195.4-6.2°. ¹⁰

4-Cl·SO₂·C₆H₄OPO₂. XI. Crystals, m. 150-1° (from benzene). ⁶

3. AMIDES OF METAPHOSPHORIC ACID

Et₂NPO₂. Probably trimeric, normally. VIIIA. Crystals, m. 103°. ⁵⁸

Pr₂NPO₂. Probably trimeric. VIIIA. Viscous oil, b₁₀ 240°. ⁵⁸

iso-Bu₂NPO₂. Probably trimeric. VIIIA. Crystals, m. 79°, b₁₅ 255°. The highest member obtained in pure state. ⁵⁸

4. ESTERS OF MONO- AND TRITHIOMETAPHOSPHORIC ACID

EtOPSO(?). Claimed to be preparable by action of sulfuric acid on triethyl thionophosphate. ³⁸ Oil.

PhCH₂SPS₂. IX. Crystals, dec. 75-6°. ⁷⁴

PhSPS₂. IX. XVII. Crystals, m. 165°. ⁷⁴

4-MeC₆H₄SPS₂. XVII. Crystals, m. 205-6°. ⁷⁴

PHOSPHONO-ANHYDRIDES OR METAPHOSPHONIC ACIDS

iso-AmPO₂. XII. Crystals, m. 122° (from ligroin). ⁴¹

PhPO₂. XII. Crystals, m. 100° (from benzene). ⁶⁰

2-MeC₆H₄PO₂. XII. Prisms (from benzene). ⁵⁴

4-MeC₆H₄PO₂. XII. Crystals, m. 101°. ⁶⁰

4-EtC₆H₄PO₂. XII. Crystals, m. 68°. ⁵⁴

4-PhCH₂C₆H₄PO₂. XII. Crystals, m. 169°. ⁵⁷

4-ClC₆H₄PO₂. XII. Crystals, m. 211° (from benzene). ⁵⁴

4-BrC₆H₄PO₂. XII. Crystalline powder, m. 185-6°. ⁵⁶

4-MeOC₆H₄PO₂. XII. Powder, m. 52°. ⁵⁴

- 2,4,5-Me₃C₆H₂PO₂.** XII. Prisms, m. 215–6° (from CHCl₃).^{56, 60}
2,4,6-Me₃C₆H₂PO₂. XII. Crystals, m. 215–6° (dec.; from CHCl₃).⁵⁶
(PhCH₂)₂CH·PO₂. XII. Plates, m. 151° (from benzene-ligroin).⁵⁹

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Appendix

The following pages summarize new information that has accumulated in the chemical literature during 1949, while this book was being written. The new material is subdivided into sections that correspond to the chapters of the book proper; similarly, the division is carried into the classification of methods of preparation to correspond with the usage elsewhere. Any new methods of preparation are given new numbers.

CHAPTER 1. GENERAL

In the course of the year several reviews of a rather general nature appeared in the English language. A rather brief and hardly adequate review of the newer methods of syntheses was compiled by Saunders.⁴⁵ A much more satisfactory and rather comprehensive treatment of the subject was given by Atherton.⁶ A very readable summary of the syntheses and the more common properties of several organophosphorus compounds, of special interest as insecticidal agents, has been prepared by Martin.³⁴

CHAPTER 2. PHOSPHINES AND RELATED COMPOUNDS

Trimethylphosphine has been shown to be unreactive toward carbon dioxide. However, it reacts rapidly with trimethylboron, forming an undescribed adduct. Its adduct with carbon disulfide, which melts at 114° with decomposition, is not volatile at room temperature.¹²

Adducts of trialkylphosphines with SnCl_4 , SnBr_4 , UCl_4 , and UBr_4 have been reported.³

A solution of trimethylphosphinemethylene, $\text{Me}_3\text{P}\text{---CH}_2$, has been prepared by the action of methyl-lithium or phenyl-lithium on tetramethylphosphonium iodide.⁵⁴

The synthesis of a pentavalent derivative of phosphorus, pentaphenylphosphorus, reportedly melting at 124°, from tetraphenylphosphonium iodide and phenyl-lithium by Wittig and Rieber,⁵⁵ revives the interest in such substances for the first time since the work of Grignard in the 1930's. The product yields triphenylphosphine oxide on oxidation with air, while heating results in the formation of benzene, without generation of triphenylphosphine. As may be expected, hydrogen iodide yields tetraphenylphosphonium iodide. The product is reported to be an active polymerization catalyst for monomeric styrene.⁵⁵

CHAPTER 4. PHOSPHONYL HALIDES

METHODS OF PREPARATION

II. Addition of phosphorus pentachloride to olefins

It has been reported that the addition of phosphorus pentachloride to olefins that have a terminal double bond and possess either one aryl group or two alkyl groups on the 2-carbon atom takes place normally, that is, with addition of the PCl_4 group to the 1-carbon atom. Normal alkenes with terminal double bond, however, give a reversed order of addition with the PCl_4 group going to the 2-carbon atom. No evidence is cited to support this conclusion, however. The products of the first category react normally with phosphorus pentoxide or with phosphorus pentasulfide, yielding, respectively, the unsaturated phosphonyl or thionophosphonyl dichlorides according to the method of Section XI. The products of the second mode of addition, however, do not lose hydrogen chloride, and this treatment yields the phosphonyl dichlorides of 1-chloro phosphonic acids.⁵¹

XVI. Reaction of hydrocarbons with phosphorus trichloride and oxygen

Additional information about this reaction includes the following items. The reaction does not cease, apparently, after monosubstitution, but continues yielding small amounts of disubstitution products, that is, bis-phosphonyl dichlorides. The essentially random nature of this reaction in the aliphatic series has been confirmed, and it was shown that the reaction with alkylated benzenes takes place only on the aliphatic group. Toluene yields phenylmethane derivative, whereas ethylbenzene gives only the 2-phenylethane derivative. Compounds with longer side chains yield isomer mixtures, however. The introduction of a phenyl group reduces the yield significantly so that diphenylmethane gives but a 2% yield.²⁶

The reaction is applicable to olefins, in which instance it results in formation of compounds with CCl-POCl_2 structure. Acetonitrile and nitromethane not only do not react, but actually hinder the oxidation of phosphorus trichloride (a concurrent and predominant reaction). However, their presence does not prevent the normal reaction of the reactive substances in such solutions.⁴⁸

NEW COMPOUNDS OR NEW CONSTANTS OF PREVIOUSLY KNOWN COMPOUNDS

Me_2POCl . VI. Crystals, m. $66.8-8.4^\circ$ (from benzene-ligroin).²⁷

$\text{ClCH}_2\text{CH}_2\text{POCl}_2$. XVI. Liquid, b_2 $86.5-7.0^\circ$, d_4^{20} 1.5446, n_D^{20} 1.4998.⁴⁸

$\text{EtCH(POCl}_2\text{)CH}_2\text{Cl}$. II-XI. Liquid, b_{18} $116-23^\circ$.⁵¹

$\text{MeCH(POCl}_2\text{)CH}_2\text{Cl}$. II-XI. Liquid, b. $190-218^\circ$.⁵¹

- $\text{C}_3\text{H}_5\text{ClPOCl}_2$. XVI (from propene). Liquid, b_2 85–7°, d_4^{20} 1.4615, n_D^{20} 1.4930.⁴⁸
 $\text{C}_4\text{H}_9\text{POCl}_2$. XVI (from isobutane). Liquid, b_2 55–7°, d_4^{20} 1.2639, n_D^{20} 1.4660.⁴⁸
 $\text{Me}_2\text{C}:\text{CHPOCl}_2$. II–XI. Liquid, b_{17} 99–101°, d 1.302.⁵¹
 $\text{C}_4\text{H}_9\text{ClPOCl}_2$. XVI (from butene). Liquid, b_5 85–7°, d_4^{20} 1.3950, n_D^{20} 1.4900.⁴⁸
 $\text{C}_4\text{H}_9\text{ClPOCl}_2$. XVI (from isobutylene). Liquid, b_4 78–80°. ⁴⁸
 $\text{PrCH}(\text{POCl}_2)\text{CH}_2\text{Cl}$. II–XI. Crystals, m . 39–42°, b_{20} 130–2°. ⁵¹
 $\text{C}_5\text{H}_{11}\text{POCl}_2$. XVI (from *n*-pentane). Liquid, b_2 67–9°, d_4^{20} 1.2180, n_D^{20} 1.4694.⁴⁸
 $\text{C}_5\text{H}_{11}\text{POCl}_2$. XVI (from 2-methylbutane). Liquid, b_2 64–5°, d_4^{20} 1.2246, n_D^{20} 1.4708.⁴⁸
 $\text{C}_6\text{H}_{13}\text{POCl}_2$. XVI (from *n*-hexane). Liquid, b_3 82–4°. ⁴⁸
 $\text{C}_6\text{H}_{13}\text{POCl}_2$. XVI (from 2,3-dimethylbutane). Liquid, b_2 75–6°, d_4^{20} 1.1733, n_D^{20} 1.4715.⁴⁸
 $\text{C}_7\text{H}_{15}\text{POCl}_2$. XVI (from *n*-heptane). Liquid, b_2 96–8°, d_4^{20} 1.1852, n_D^{20} 1.4830.⁴⁸
 $\text{C}_8\text{H}_{17}\text{POCl}_2$. XVI (from 2,2,4-trimethylpentane). Liquid, b_2 81–2°, d_4^{20} 1.1329, n_D^{20} 1.4707.⁴⁸
 $\text{Me}_3\text{CCH}_2\text{CMe}:\text{CHPOCl}_2$. II–XI. Liquid, b_{13} 128–9°, d^{25} 1.129.⁵¹
 $\text{PhCH}:\text{CHPOCl}_2$. II–XI. Crystals, m . 70°, b_{18} 182–4°. ⁵¹
 $\text{C}_6\text{H}_{11}\text{POCl}_2$. XVI (from cyclohexane). Crystals, m . 39–40°, b_2 93–4°. ⁴⁸
 $\text{PhCH}:\text{CHPSCl}_2$. II–XI. Liquid, b_8 162–5°, d^{26} 1.345.⁵¹

The following, presumably para-isomers, have been reported:

- $\text{MeC}_6\text{H}_4\text{POCl}_2$. XI. Liquid, b_{11} 140–2°. ⁵²
 $\text{ClC}_6\text{H}_4\text{POCl}_2$. XI. Liquid, b_{4-5} 104–5°. ⁵²

CHAPTER 5. QUATERNARY PHOSPHONIUM COMPOUNDS

METHODS OF PREPARATION

XIV. Addition reactions of phosphinemethylenes

It has been shown that phosphinemethylenes add alkyl halides, forming quaternary phosphonium halides.⁵⁴

XVI. Reaction of organolithium compounds with quaternary phosphonium compounds and with tertiary phosphine oxides

Prolonged action of phenyl-lithium on triphenylphosphine oxide, followed by treatment with hydrogen halide, yields tetraphenylphosphonium halides. Phenyl-lithium reacts slowly with tetramethylphosphonium iodide yielding mono- or disubstituted derivatives that react with benzophenone, forming the corresponding phosphonium halides containing 1- or 2-diphenyl-2-hydroxyethyl groups. The formation of such compounds indicates the probable intermediate formation of the corresponding phosphinemethylenes.^{54, 55}

NEW COMPOUNDS OR CONSTANTS ON PREVIOUSLY KNOWN SUBSTANCES

- Ph_4PCl . XVI. Poorly stable solid, m . 65–75°. ^{54, 55}
 Ph_4PI . XV. Crystals, m . 330–40°. ^{54, 55}
 Me_3EtPI . XIV. Crystals, m . 310–30°. ⁵⁴

Et₄PI. By prolonged action of PhLi on Me₄PI, which yields some unisolated (LiCH₂)₂PCH₂, followed by treatment with MeI.⁵⁴
(HOCPH₂CH₂)Me₃PI. XVI (from Me₄PI and PhLi, followed by Ph₃CO and KI). Crystals, m. 200–40°.⁵⁴ On heating, regenerates Me₄PI.⁵⁴

CHAPTER 6. TERTIARY PHOSPHINE OXIDES

Ph₂P(O)CCl₃. III. Crystals, m. 138–9° (from EtOH).²⁸

CHAPTER 7. PHOSPHONOUS, PHOSPHONIC, AND PHOSPHINOUS ACIDS AND THEIR ESTERS

METHODS OF PREPARATION

IA. Reactions of esters of trivalent phosphorus with halides.

It has been shown that the phenyl esters of trivalent phosphorus do not undergo the Arbuzov-Michaelis reaction with carbon tetrachloride.²⁸

Although 1,4-dichloro-2-butene reacts with trialkyl phosphites normally, yielding the corresponding diphosphonates, the reaction of 1,2-dichloro-3-butene yields only unworkable resins.⁴⁰ The action of 5-chloro-1-methoxy-3-pentene with trialkyl phosphites is normal, but 3-chloro-1-methoxy-4-pentene reacts with an apparent allylic shift and similarly yields the 5-phosphono derivatives.⁴¹

IB. Reaction of metal salts of dialkyl phosphites with halides.

Although sodium (or potassium) dialkyl phosphites react with 5-chloro-1-methoxy-3-pentene normally, the reaction with the isomeric 3-chloro-1-methoxy-4-pentene may take two courses. If an excess of free dialkyl phosphite is present, an allylic shift results in the formation of the 5-phosphono derivative. In the absence of the free ester, however, a molecule of the sodium dialkyl phosphite adds to the double bond of the primary reaction product and yields the corresponding diphosphonate. The addition takes place in both possible orientations, and the resulting sodio derivative reacts with the halide present in the mixture, forming a butadiene derivative and the mixture of isomeric diphosphonates.⁴¹

IVC. Reaction of hypophosphorous acid (or phosphonous acids) with carbonyl compounds and primary amines. The reaction of hypophosphorous acid with primary amines, followed by heating with an aldehyde or ketone, results in the formation of phosphonous acids of the substituted amino type, carrying the radical of the amine and the phosphorus atom on the carbon of the original carbonyl group. Secondary amines do not react.⁴⁶ Acetone was the carbonyl compound used in most of the reported preparations.

V. Reaction of Grignard reagents with phosphorus halides

Reaction of methylmagnesium iodide with PSCl_3 results in the formation of a dimer, $\text{Me}_2\text{P}-\text{PMe}_2\cdot\text{S}_2$, which on oxidation yields the expected dimethylphosphonic acid. The nature of the dimer is not clear, but it should be noted that its formation appears to confirm the lack of reactivity of the thiophosphoryl chloride with Grignard reagents in the normally expected sense, that is, with formation of tertiary phosphine sulfides, when the radicals of the Grignard reagent are the lower alkyls.²⁷

VI. Oxidative phosphonation

The reaction of hydrocarbons with phosphorus trichloride in the presence of oxygen was discussed in Chapter 4, XVI heading. Since many of the phosphonyl chlorides so obtained are directly hydrolyzed to the acids, the summary of new developments given there is deemed sufficient.^{26, 48}

General characteristics. It was shown that esters of phenylmethanephosphonic acid are nitrated exclusively in the para position, but the derivatives of benzenephosphonic acid yield not only the meta-nitro esters, but also appreciable amounts of the ortho isomers, and, possibly, the para isomers.^{30, 31} The previous reference to the work of Limaye and Bhide noted by an asterisk in the previous list of compounds may be augmented at this time by reference to a published paper.³³

NEW COMPOUNDS

PHOSPHONOUS ACIDS AND THEIR ESTERS

- EtP(OPh)₂.** XV. Liquid, b_{11} 223–5°, d^0 1.1923, n^{16} 1.5912.²⁸
PhP(OPh)₂. XV. Liquid, b_8 220°, d^0 1.1649, n^{16} 1.6101.²⁸
4-MeOC₆H₄P(OEt)₂. XV. Liquid, b_{13} 136–8°, d^0 1.0529, d^{16} 1.0433, n^{16} 1.4986.²⁸
PhNHCM₂PO₂H₂. IVC. Crystals, decomp. 214°. ⁴⁶
4-AcNHC₆H₄NHCM₂PO₂H₂. IVC. Crystals, decomp. 216° (dihydrate). ⁴⁶
4-H₂NSO₂C₆H₄NHCM₂PO₂H₂. IVC. Crystals, decomp. 200°. ⁴⁶
4-H₂NSO₂C₆H₄CH₂NHCM₂PO₂H₂. IVC. Crystals, decomp. 232°. ⁴⁶
PrNHCM₂PO₂H₂. IVC. Crystals, decomp. 227°. ⁴⁶
C₆H₁₁NHCM₂PO₂H₂. IVC. Crystals, decomp. 217°. ⁴⁶
H₂N(HN:)CNHNHCM₂PO₂H₂. IVC. Crystals, decomp. 186°. ⁴⁶
PhNHNHCM₂PO₂H₂. IVC. Crystals, decomp. 165°. ⁴⁶
4-EtOC₆H₄NHCM₂PO₂H₂. IVC. Crystals, decomp. 189°. ⁴⁶
PhNHCHMePO₂H₂. IVC. Crystals, decomp. 190°. ⁴⁶
SO(C₆H₄NHCHMePO₂H₂)₂. IVC. Isolated as the sodium salt. ⁴⁶
3-Cl-4-AcNHC₆H₄NHCM₂PO₂H₂. IVC. Crystals, decomp. 200°. ⁴⁶
4-AcNHC₆H₄NHCM₂EtPO₂H₂. IVC. Crystals, decomp. 142° (dihydrate). ⁴⁶
4-EtOC₆H₄NHCM₂PhPO₂H₂. IVC. Crystals, decomp. 167°. ⁴⁶
2-HOC₆H₄CH(NHCH₂Ph)PO₂H₂. IVC. Crystals, m. 225°. ⁴⁶
PhCH(NHPh)PO₂H₂. IVC. Crystals, decomp. 150°. ⁴⁶

(:AsC₆H₃(OH)NHCMe₂PO₂H₂)₂. IVC. Crystals; isolated as sodium salt.⁴⁶

OCNPhNMeCMe:CNHCMe₂PO₂H₂. IVC. Crystals, decomp. 185°.⁴⁶

SCH:CHN:CNHSO₂C₆H₄NHCMe₂PO₂H₂. IVC. Crystals, decomp. 184°.⁴⁶

PHOSPHONIC ACIDS AND ESTERS

PRIMARY PHOSPHONIC ACIDS AND ESTERS

CH₂:CMeCOPO(OEt)₂. IA. Undistillable oil.³⁰

AcPO(OEt)₂. IA. Liquid, b₂₀ 114–5°, b₄ 83°, n_D²⁰ 1.4200.³⁰

Me₂C:CHPO(OEt)₂. XV. Liquid, b₅ 107°, d 1.038, n 1.441.⁵¹

PrCH(PO(OBu)₂)CH₂Cl. XV. Liquid, b₄ 154–62°, d²⁵ 1.106.⁵¹

Me₃CCH₂PO(OH)₂. VI–XVI. Crystals, m. 140–40.5° (from CCl₄).³⁶

MeOCH₂PO(OCH₂CH₂OMe)₂. IA. Liquid, b₇ 154–6°, b₁₃ 163–4°, n_D²⁰ 1.4375, d₀²⁰ 1.1456.¹

MeOCH₂PO(OCH₂CH₂OEt)₂. IA. Liquid, b_{3,5} 155–6°, n_D²⁰ 1.4345, d₀²⁰ 1.0877.¹

EtOCH₂PO(OCH₂CH₂OMe)₂. IA. Liquid, b₁₃ 168–9.5°, d₀²⁰ 1.1258, n_D²⁰ 1.4373.¹

EtOCH₂PO(OCH₂CH₂OEt)₂. IA. Liquid, b₁₁ 168–70°, n_D²⁰ 1.4340, d₀²⁰ 1.072.¹

PrOCH₂PO(OCH₂CH₂OMe)₂. IA. Liquid, b_{3,5} 157–9°, n_D²⁰ 1.4389, d₀²⁰ 1.101.¹

PrOCH₂PO(OCH₂CH₂OEt)₂. IA. Liquid, b₃ 158.5–59°, n_D²⁰ 1.4364, d₀²⁰ 1.055.¹

MeOCH₂CH₂PO(OCH₂CH₂OMe)₂. IA. Liquid, b₈ 155–6.5°, n_D²⁰ 1.4392, d₀²⁰ 1.1435.¹

EtOCH₂CH₂PO(OCH₂CH₂OEt)₂. IA. Liquid, b₉ 183–4°, n_D²⁰ 1.4372, d₀²⁰ 1.069.¹

CH₂:CHO₂CCH₂PO(OEt)₂. IA. Liquid, b_{2,5} 117–9°, n_D²⁴ 1.4431, d₀²⁵ 1.1370.¹⁹

MeOCH₂CH₂CH:CHCH₂PO(OEt)₂. IA. IB. Liquid, b₈ 146–7°, n_D²⁰ 1.4480, d₄²⁰ 1.0380. Best made by IA.⁴¹

MeOCH₂CH₂CH:CHCH₂PO(OBu-iso)₂. IA. IB. Liquid, b₃ 145–6°, n_D²⁰ 1.4455, d₄²⁰ 0.9819.⁴¹

MeOCH₂CH₂CH:CHCH₂PO(OMe)₂. IA. IB (very poor yield). Liquid, b₁₀ 144°, n_D²⁰ 1.4530, d₄²⁰ 1.0950.⁴¹

PhCH₂PO(OH)₂. VI–XIII. Crystals, m. 167.4–69° (from water).³⁶

PhCH₂CH₂PO(OH)₂. IA–XIV. VI–XIII. Crystals, m. 136.5–8°.³⁶

Ph₂CHPO(OH)₂. VI–XIII. Crystals, m. 234–7°.³⁶

PhCH:CHPO(OPh)₂. XV. Crystals, m. 109°.⁵¹

PhCH:CHPO(OCH₂CH₂EtBu)₂. XV. Liquid, b₃ 238–40°.⁵¹

4-O₂NC₆H₄CH₂PO(OBu)₂. By nitration of the corresponding ester. Liquid, b₃ 210–1°, n_D²⁸ 1.5058.³⁰ Free acid, m. 226°.³⁰

PhCH₂P(O)OCMe₂CMe₂O. IA. Crystals, m. 115–6.3°.⁵

Ph₃CP(O)OCMe₂CMe₂O. IA. Crystals, m. 231–1.5°.⁵

BzP(O)OCMe₂CMe₂O. IA. Crystals, m. 90–1°; 2,4-dinitrophenylhydrazone, m. 194.5–5.5°.⁵

(:CHCH₂P(O)(OEt)₂)₂. IA. IB. Liquid, b₁₅ 226°, n_D²⁰ 1.4547, d₄²⁰ 1.1247.⁴⁰

MeOCH₂CH₂CH(PO(OEt)₂)CH₂CH₂PO(OEt)₂. IB. Liquid, b₁₀ 238–46°, n_D²⁰ 1.4600.⁴¹

MeOCH₂CH₂CH₂CH(PO(OEt)₂)CH₂PO(OEt)₂. IB. Liquid, b₁₅ 222°, b₁₁ 216–7°, n_D²⁰ 1.4478, d₄²⁰ 1.1060.⁴¹

MeOCH₂CH₂CH₂CH(PO(OBu-iso)₂)CH₂PO(OBu-iso)₂. IB. Liquid, b₇ 225–9°, b₁₀ 237°, n_D²⁰ 1.4470, d₄²⁰ 1.0203.⁴¹

C₆H₁₀(PO(OH)₂)₂. VI–XIII. Decomp. 233°. Isomer structure unknown.²⁶

Me₂C(CH₂PO₃H₂)₂. VI–XIII. Crude solid, m. 160–7°. ²⁶

Di-*n*-butyl 2-indenephosphonate. XV. Liquid, b₃ 105–15°. ²

Dicyclohexyl 2-indenephosphonate. XV. Crystals, m. 87°. ²

***n*-Butyl cyclohexyl 2-indenephosphonate.** XV. Crystals, m. 85–7°. ¹

PhP(O)(OH)₂. Monothallium salt, m. 200–1°; dithallium salt, m. 317°. ²⁸

3-H₂NC₆H₄PO(OH)₂. By hydrolysis of the corresponding diethyl ester, followed by separation from the 2-isomer by crystallization. Crystals, decomp. 290–2°. ²¹

SECONDARY PHOSPHONIC ACIDS AND THEIR ESTERS

Me₂PO(OH). V (from PSCl₃, followed by oxidation with nitric acid of the intermediate (Me₂PS)₂, which m. 205–13°). Needles, m. 86.5–8.5° (from dry benzene). Very weak acid. ²⁷

Ph₂PO(OH). Thallium salt, m. 203–5°. ²³

Ph₂PO(OEt). The rather high melting point given to this by Michaelis justifies re-examination of this substance. (Author.)

(4-MeOC₆H₄)(Cl₃C)PO(OEt). IA. Liquid, b₄ 145–7°, d₀⁰ 1.2815, d₀¹⁶ 1.2650, n_D¹⁶ 1.5068. ²³

(4-MeC₆H₄)(Cl₃C)PO(OH). XV. Crystals, hydrolyzed to PhPO₃H₂ by a long hydrolysis with water. ²³

Methyl ester. IA. Liquid, b₂₋₄ 128–9°, d₀⁰ 1.2328, n_D²⁰ 1.5312. ²³

Ethyl ester. IA. Liquid, b₂₋₄ 157–8°, d₀⁰ 1.3260, n_D²⁰ 1.5423. ²³

Propyl ester. IA. Liquid, b₂₋₄ 168–70°, d₀⁰ 1.3094, n_D²⁰ 1.5370. ²³

n-Butyl ester. IA. Liquid, b₂₋₄ 180–1°, d₀⁰ 1.2303, n_D²⁰ 1.5267. ²³

iso-Butyl ester. IA. Liquid, b₂₋₄ 178–80°, d₀⁰ 1.2661, n_D²⁰ 1.5294. ²³

SECONDARY PHOSPHINOUS ACID DERIVATIVES

Ph₂OEt. XV. Liquid, b₁₃ 176–7°. ²⁸

THIOPHOSPHONIC ACID DERIVATIVES

PhCH:CHPS(OPh)₂. XV. Crystals, m. 83°. ⁵¹

CHAPTER 8. PHOSPHITES AND HALOPHOSPHITES

METHODS OF PREPARATION

I. Reaction of phosphorus trihalides with alcohols

Berlak and Gerrard have shown that phosphorus tri-iodide reacts with aliphatic alcohols at low temperature, largely with the formation of the corresponding alkyl iodides, although small amounts of unisolated phosphorus compounds also form. The reaction mechanism is similar to the one shown by the trichloride or the tribromide studied earlier. A successive four-center reaction yields the tertiary ester, which coordinates with the proton of the resulting hydrogen iodide, and the iodide ion removes an alkyl group with inversion. ¹⁰

The reactions of glycols were investigated further. Arbuzov and Azanovskaya found that phosphorus trichloride and pinacol yield the expected cyclic chlorophosphite, which is remarkably stable to hydrolysis and preserves the cyclic structure through various isomerization reac-

tions.⁵ An excess of ethylene glycol in the reaction with phosphorus trichloride yields a cyclic secondary diphosphite. Although the evidence for the structure is indirect, the compound seems to be almost certainly $\text{HOP}(\text{OCH}_2\text{CH}_2\text{O})_2\text{POH}$.¹⁵

When phosphorus dichlorofluoride is used in esterifications, the chlorine atoms are replaced preferentially, thus yielding fluorophosphites.¹⁵

VII. Reaction of phosphites with tertiary bases

A rather useful reaction was discovered recently by the Cambridge group, headed by Todd. It was found that neutral phosphites containing a benzyl group, which may or may not be substituted, lose this group on being heated with a tertiary base (N-methylmorpholine or triethylamine appear to be most satisfactory) at reflux for a few hours. The loss of benzyl groups is stepwise, only one being lost at a time. Thus tribenzyl phosphite yields dibenzyl phosphite, whereas the latter yields some monobenzyl phosphite only if the reaction is run in separate steps. It is suggested that only the keto form of the ester can react and that the degradation of the tertiary ester stops after conversion to the secondary ester because the latter exists in the reaction mixture in the form of an ionic salt with the base; the ionic form based on the enol form is incapable of further reaction.⁷

General information. An attempt was made by another Cambridge group to investigate the extent of the keto-enol equilibrium in various secondary phosphites. The method used was based on the time necessary for the disappearance of phenolphthalein color when small successive additions of aqueous alkali were made to the various phosphites. If it is assumed that only the enol form can form a water-soluble salt, the results indicate that many of the dialkyl phosphites (for example, diethyl) exist partly in the enol form, but dicyclohexyl phosphite, being alkali-insoluble, is an example of completely keto structure.¹⁵ Unfortunately, evidence of this kind does not take into account the different rates of hydrolysis of the esters by the alkaline media, which would also give different periods of indicator color disappearance. Neither does it take into account the rather convincing evidence from the physical investigations, such as the parachor, that indicate that the secondary phosphites are hydrogen-bonded dimers or trimers, without a real keto-enol system.

NEW COMPOUNDS OR NEW CONSTANTS OF PREVIOUSLY KNOWN COMPOUNDS

HALOPHOSPHITES

EtOPCl₂. I. Liquid, b. 117–8°.¹⁶

(EtO)₂PF. I (from PFCl_2). Liquid, b₁₈ 80–1.5°. On being heated with alcoholic NaOH, the compound loses F in preference to ester group hydrolysis.¹⁶

(EtO)₂PCl. II. IV. Liquid, b_{15} 45–53°, b_{18} 34–42°, b 143–8°.¹⁵ The wide boiling ranges appear to indicate a non-homogeneous ester. The compound is unreactive toward KCN or NaF.¹⁵

OCMe₂CMe₂OPCl. I. Liquid, b_{13} 81.5–2.0°, d_0^{20} 1.1562, n_D^{20} 1.4720.⁵

PRIMARY PHOSPHITES

PhCH₂OPO₂H₂. VII. Oil. Best isolated as the ammonium salt, needles, m 154° (from dioxan-EtOCH₂CH₂OH).⁷

SECONDARY PHOSPHITES

(FCH₂CH₂O)₂POH. I. Liquid, $b_{1.7}$ 109–10°.¹⁵

(ClCH₂CH₂O)₂POH. I. Liquid, $b_{0.6}$ 129°.¹⁶

(MeEtCHO)₂POH. I. Liquid, b_{15} 111°.¹⁶

(C₆H₁₁O)₂POH. I. Liquid, $b_{0.6}$ 135–43°, $b_{0.15}$ 120°.¹⁵

OCMe₂CMe₂OPOH. I. VIII. Hygroscopic crystals, m 106.5–8° (from petroleum ether).⁵

HOP(OCH₂CH₂O)₂POH. I. Liquid, $b_{0.15}$ 99.5°.¹⁵

TERTIARY PHOSPHITES

(FCH₂CH₂O)₃P. II. Liquid, b_8 114–6°, d_{20}^{20} 1.285, n_D^{20} 1.417.²⁹

(MeOCH₂CH₂O)₃P. II. Liquid, b_8 138.5–40°, n_D^{20} 1.4402, d_4^{20} 1.096.¹

(EtOCH₂CH₂O)₃P. II. Liquid, b_9 156–8°, n_D^{20} 1.4377, d_4^{20} 1.034.¹

(PhCH₂O)₃P. II. Crude oil, $b_{0.05}$ 225–30°. Oxidizes in air to the phosphate.⁷

(PhO)₃P. I. Liquid, b_{11} 218–9°. ²⁸

***o*-C₆H₄O₂POEt.** II. Liquid, b_{19} 99–100°. ¹⁵

OCMe₂CMe₂OPOMe. II. Liquid, b_{48} 91–2.5°, d_0^0 1.0622, d_0^{80} 1.0449, d_{20}^{20} 1.0469, n_D^{20} 1.4417.⁵

OCMe₂CMe₂OPOEt. II. Liquid, b_{14} 75–6°, d_0^0 1.0322, d_0^{20} 1.0136, d_{20}^{20} 1.0156, n_D^{20} 1.4392.⁵

OCMe₂CMe₂OPOPr. II. Liquid, $b_{11.5}$ 84.5–6.0°, d_0^0 1.0138, d_0^{20} 0.9961, d_{20}^{20} 0.9981, n_D^{20} 1.4392.⁵

OCMe₂CMe₂OPOBu. II. Liquid, $b_{14.5}$ 105–6.5°, d_0^0 1.0076, d_0^{20} 0.9901, d_{20}^{20} not cited, d_{20}^{20} 0.9780, n_D^{20} 1.4413.⁵

CHAPTER 9. PHOSPHATES AND RELATED COMPOUNDS

METHODS OF PREPARATION

Q. Chlorination of derivatives of dithiophosphoric acid

It was found that dialkyl thiochlorophosphates, (RO)₂PSCl, may be readily formed by treatment of compounds of the general type ((RO)₂PS)₂S_{*n*} with chlorine, sulfur monochloride, or sulfur dichloride.⁴

X. Reaction of sodium phenoxides with thiochlorophosphates

The reaction of (RO)₂PSCl with solid sodium phenoxides, which is

very sluggish in neutral, organic solvents, is accelerated by the presence of moderate amounts of tertiary organic bases.⁵⁰

XVIIC. Reaction of tertiary esters with tertiary bases. On being refluxed with a tertiary base (N-methylmorpholine or triethylamine) tertiary esters containing benzyl (substituted or unsubstituted) groups lose one of these radicals in a very smooth reaction.⁷

General characteristics. Hydrolysis of phosphates that possess a carbonyl group displays a rate minimum in the range of pH 3–4, whereas esters without such carbonyl substitution have a maximum hydrolysis rate at approximately the same pH range (4–5), as shown by hydrolysis of diose phosphate on one hand and that of ethyl phosphate on the other.²¹

NEW COMPOUNDS

HALOPHOSPHATES

- FCH₂CH₂OPOCl₂.** A. Liquid, *b*₃₀ 106–7°, *d*₂₀²⁰ 1.5367, *n*_D²⁰ 1.4400.²⁹
2-MeOC₆H₄OPOCl₂. A. Liquid, *b*₃ 126–9°.³²
(ClCH₂CH₂O)₂POF. D. Liquid, *b*_{0.8} 107°, ¹⁵ *b*₁₅ 142°.¹⁶
(ClCH₂CH₂O)₂POCl. B. Liquid, *b*_{0.6} 122–4°, ¹⁵ *b*_{2.3} 139°.¹⁶
(EtO)₂POCNS. D. Poorly stable liquid, *b*₁ 80–2°.¹⁵
((ClCH₂)₂CHO)₂POF. D. Liquid, *b*_{0.7} 163–5°.¹⁶
(MeEtCHO)₂POF. D. Liquid, *b*_{0.8} 62–4°, *b*_{0.15} 64.5°.¹⁶
(MeEtCHO)₂POCl. B. Liquid, *b*_{0.8} 92–4°.¹⁶
(BuO)₂POF. F. Liquid, *b*₃₀ 128°.¹⁶
(AmO)₂POF. F. Liquid, *b*₃₀ 143–4°.¹⁶
(iso-AmO)₂POF. D. F. Liquid, *b*₂₈ 142°, *b*₂₃ 135–8°.¹⁶
(Et₂CHO)₂POF. D. Liquid, *b*₂ 97–8°.¹⁶
(Me₂CHCH₂CHMeO)₂POF. D. Liquid, *b*_{2.7} 102–3°.¹⁶
(EtO₂CCHMeO)₂POF. D (with AgF). Liquid, *b*_{0.6} 126–8°.¹⁶
(2-MeOC₆H₄O)₂POCl. A. Crystals, *m.* 65–7°, *b*₃ 213–5°.³²

PRIMARY PHOSPHATES

- OHCCH₂OPO(OH)₂.** By oxidation of 1-glycerophosphate with HIO₄. Barium salt (tetrahydrate).²¹
Glucose-4-phosphate. IV–XVIIIB (from 1,2,3,6-tetra-acetyl derivative). Disodium salt, crystals, decomp. 155°, [*α*]_D²⁰ 51.5° (in H₂O). Dibrucine salt, *m.* 173–4°.⁴²
Inositol-5-phosphate. IV–XVIIIB (from penta-acetyl derivative). Disodium salt, *m.* 233–4° (from EtOH-ligroin). Free acid, *m.* 198–200°.³⁵
Scyllitol monophosphate. IV–XVIIIB (analogously to the above). Free acid, *m.* 212–4°; disodium salt, solid.³⁵
Adenosine-2'-phosphate. IV–XVIIIB (from benzylidene derivative). Free acid, decomp. 205–15°; dibrucine salt, *m.* 165–75°; acridine salt, *m.* 215° (decomp.).³⁵
Adenosine-3'-phosphate. IV–XVIIIB (from trityl-2'-acetyl derivative). Free acid, *m.* 194°, is identical with the natural yeast adenylic acid. Dibrucine salt, *m.* 177°; acridine salt, dec. 175°.³⁵
Guanosine-2'-phosphate. IV–XVIIIB (from 3',5'-benzylidene derivative). Free acid, decomp. 192°.³⁵

- Guanosine-5'-phosphate.** VII-XVIIIB (from 2',3'-isopropylidene derivative). Free acid, decomp. 190–200°. Dibrucine salt, decomp. 210°. The results indicate that the natural guanylic acid is the 3'-phosphate.³⁵
- Uridine-3'-phosphate.** IV-XVIIIB (from 2'-acetyl-5'-trityl derivative or from 5'-trityl derivative). Free acid, m. 192°. Dibrucine salt, m. 182–7°. The product is identical with natural uridylic acid.³⁵
- Uridine-5'-phosphate.** IV-XVIIIB (from 2',3'-isopropylidene derivative). Isolated as the barium salt, plates. Dibrucine salt, m. 185–90°. ³⁵
- Cytidine-2'-phosphate.** IV-XVIIIB (from 3',5'-benzylidene derivative). Free acid, decomp. 235°. Hydrolysis with dil. H₂SO₄ is analogous to that shown by other 2'-nucleotides, that is, the rate is intermediate between the 3'- and the 5'-isomers. Probably Gulland-Smith product (*J. Chem. Soc.*, 1948, 1527) was impure.³⁵
- Cytidine-5'-phosphate.** IV-XVIIIB (from 2',3'-benzylidene derivative). Free acid, plates, decomp. 233°. Dibrucine salt, decomp. 215°. ³⁵
- D-Ribofuranose-5-phosphate.** IV-XVIIIB (from 2',3'-isopropylidene derivative). Isolated as the barium salt. Free acid has $([\alpha]_D^{15})$ 16.5° (in dil. HCl).³⁵
- PhOPO(OH)₂.** Silver salt, crystals. Complex with diethylgold, crystals, m. 130°. ²² Cyclohexylamine salt, m. 214–5°. ⁷

SECONDARY PHOSPHATES

- (iso-AmO)(PhCH₂O)PO(OH).** XVIIC. Silver salt. ⁷ Cyclohexylamine salt, crystals, m. 131–2° (from Me₂CO). ⁷
- (PhCH₂O)₂PO(OH).** XVIIC. Crystals, m. 79–80°. Cyclohexylamine salt, m. 173°. ⁷
- (PhCH₂O)(C₆H₁₁O)PO(OH).** XVIIC. Silver salt. ⁷
- (4-BrC₆H₄CH₂O)₂PO(OH).** XVIIC. Needles, m. 155–6°. Silver salt. ⁷
- (4-O₂NC₆H₄CH₂O)₂PO(OH).** XVIIC. Crystals, m. 173–4°. Silver salt. ⁷
- (PhCH₂O)(PhO)PO(OH).** XVIIC. Oil. Cyclohexylamine salt, m. 145°. ⁷
- (PhO)₂PO(OH).** Silver salt, crystals. Complex with diethylgold, solid, m. 70–1°. ²²
- (4-O₂NC₆H₄CH₂O)(2-HOC₆H₁₀O)PO(OH).** Undescribed, XVIIC.
- Di-(5-chloro-2,3-1',3'-dioxatetramethylenebenzyl) phosphate.** XVIIC. Needles, m. 183–4°. ⁷

TERTIARY PHOSPHATES

- (FCH₂CH₂O)₃PO.** VI. Liquid, b₁₁ 169°, d₂₀²⁰ 1.365, n_D²⁰ 1.4043. ²⁹
- (EtO)(4-O₂NC₆H₄CH₂O)₂PO.** V. Needles, m. 65–6°. ⁷
- (4-O₂NC₆H₄CH₂O)₃PO.** V (in MeCN). Crystals, m. 127–8°. ⁷
- (4-BrC₆H₄CH₂O)₃PO.** V (in MeCN). Crystals, m. 132–3°. ⁷
- (PhCH₂O)₂(2-HOC₆H₁₀O)PO.** V. XII. Needles, m. 78–80°. ⁷
- (4-O₂NC₆H₄CH₂O)₂(2-HOC₆H₁₀O)PO.** V. XII. Needles, m. 112–3°. ⁷
- (4-BrC₆H₄CH₂O)₂(2-HOC₆H₁₀O)PO.** V. XII. Crystals, m. 104–5°, or 112–3°. ⁷
- Tri-(5-chloro-2,3,1',3'-dioxatetramethylenebenzyl) phosphate.** V. Solid, m. 142–3° or 157–8°. ⁷
- (PhCH₂O)₂(PhO)PO.** X. Crystals, m. 42°. ⁷
- (2-MeOC₆H₄O)₃PO.** XI. Crystals, m. 90–1°, b₃ 275–80°. ²²
- (Et₂AuO)₃PO.** V (using Et₂AuBr). Needles, m. 123°. ²²
- (Bu₃AuO)₃PO.** V (using ethylenediaminodibutylgold bromide). Crystals, m. 114°. ²²

CHAPTER 10. COMPOUNDS WITH PHOSPHORUS TO NITROGEN LINK

No truly new procedures have been reported in this section. It has been shown, however, that reactions of N-arylamidodichlorophosphates with ammonium hydroxide, followed by acidification, yield not the N-arylamidophosphates but rather the diamido derivatives of the general type $\text{ArNHPO}(\text{NH}_2)\text{OH}$.⁴⁴ Much more work is necessary to establish the generality of this reaction, although some earlier indications of such transformation have been pointed out in this chapter, Section XXIII.

NEW COMPOUNDS

HALOAMIDOPHOSPHATES

- $\text{Me}_2\text{NPOCl}_2$. III. Liquid, b_{18} 88° .¹⁷
 $(\text{Me}_2\text{N})_2\text{POCl}$. II. Liquid, b_6 102° ,¹⁷ b_{30} $133-4^\circ$, $b_{0.6}$ $79-82^\circ$.¹⁵
 $(\text{Me}_2\text{N})_2\text{POF}$. XX (using ZnF_2). Liquid, b_{15} $92-3^\circ$.¹⁵
 $(\text{PhNH})_2\text{POCl}$. II. Crystals, m. 167° (from EtOH).¹⁵
 $(\text{PhNH})_2\text{POF}$. XX. Crystals, m. 144° (from EtOH).¹⁵
 $(4\text{-ClC}_6\text{H}_4\text{NH})\text{POCl}_2$. II. Crystals, m. $105-7^\circ$ (from benzene).⁴⁴
 $(\text{EtO})(\text{Me}_2\text{N})\text{POCl}$. II. Liquid, b_{18} $98-100^\circ$.¹⁵
 $(\text{EtO})(\text{Me}_2\text{N})\text{POF}$. XX. Liquid, b_{18} $76-8^\circ$.¹⁵
 $(\text{EtO})(\text{PhNH})\text{POF}$. II. Solid, m. about 50° (from AcOH), $b_{0.2}$ $100-50^\circ$.¹⁵

AMIDOPHOSPHATES AND RELATED COMPOUNDS

- $\text{PhNHPO}(\text{OH})_2$. By hydrogenation of the dibenzyl ester. Crystals, m. $276-7^\circ$.¹⁵
 $\text{EtO}_2\text{CCH}_2\text{NHPO}(\text{OPh})_2$. II. Crystals, m. $77-8^\circ$.⁴⁷
 $\text{EtO}_2\text{CCH}(\text{CH}_2\text{Ph})\text{NHPO}(\text{OPh})_2$. II. Crystals, m. $78-9^\circ$.⁴⁷
 $\text{EtO}_2\text{CCH}_2\text{CH}_2\text{CH}(\text{CO}_2\text{Et})\text{NHPO}(\text{OPh})_2$. II. Crystals, m. $73.5-4^\circ$. This and the two preceding compounds are remarkably stable to hydrolysis.⁴⁷
 $(\text{Me}_2\text{N})_2\text{PO}(\text{OEt})$. X. Liquid, b_8 93.5° .¹⁷
 $\text{PhCH}_2\text{NHPO}(\text{OPh})_2$. II. Crystals, m. $101-2.5^\circ$ (from EtOH).³²
 $\text{PhNHPO}(\text{OPh})_2$. II. Crystals, m. $129-30^\circ$.³² This and the preceding compound could not be de-esterified by hydrogenation.³²
 $\text{PhNHPO}(\text{OC}_6\text{H}_4\text{OMe-}o)_2$. II. Crystals, m. $129-30^\circ$.³²
 $\text{PhNHPO}(\text{OEt})_2$. Described earlier.¹⁵
 $\text{PhNHPO}(\text{OCH}_2\text{CH}_2\text{F})_2$. II. Crystals, m. $68-70^\circ$.¹⁵
 $4\text{-O}_2\text{NC}_6\text{H}_4\text{NHPO}(\text{OPh})_2$. II. Crystals, m. $146.5-7.5^\circ$.³²
 $2\text{-EtO}_2\text{CC}_6\text{H}_4\text{NHPO}(\text{OPh})_2$. II. Crystals, m. $148.5-9^\circ$.³²
 $4\text{-EtO}_2\text{CC}_6\text{H}_4\text{NHPO}(\text{OC}_6\text{H}_4\text{OMe-}o)_2$. II. Crystals, m. $108-9^\circ$.³²
 $\text{C}_6\text{H}_{10}\text{NPO}(\text{OPh})_2$. II. Crystals, m. $75-6^\circ$ (from dil. MeOH).³²
 $\text{C}_6\text{H}_{10}\text{NPO}(\text{OC}_6\text{H}_4\text{OMe-}o)_2$. II. Crystals, m. $55-6^\circ$ (from Et_2O).³²
 $4\text{-Me}_2\text{NC}_6\text{H}_4\text{NHPO}(\text{OEt})_2$. II. Plates, m. 94° (from ligroin).¹⁵
 $4\text{-Me}_2\text{NC}_6\text{H}_4\text{NHPO}(\text{OCH}_2\text{Ph})_2$. XXVII. Crystals, m. $123-4^\circ$.¹⁵
 $(o\text{-C}_6\text{H}_4\text{N})\text{NHSO}_2\text{C}_6\text{H}_4\text{NHPO}(\text{OPh})_2$. II. Crystals, m. $215-6^\circ$.³²
 $4,4'\text{-(PhO)}_2\text{PONHC}_6\text{H}_4)_2\text{SO}_2$. II. Crystals, m. $232-4^\circ$.³²
 $4\text{-ClC}_6\text{H}_4\text{PO}(\text{NH}_2)\text{OH}$. From the dichloro derivative with ammonium hydroxide. Crystals, m. $156-7^\circ$.⁴⁴ The compound made by the same procedure and having

the same m.p. was given the $\text{PO}(\text{OH})_2$ structure by Otto (*Ber.*, **28**, 617 [1895]).
4,4'-(Me₂N)₂PONHC₆H₄)₂SO₂. II. Crystals.²⁴

DERIVATIVES OF PHOSPHONITRILIC CHLORIDE

(PN(OBu)₂)₃. From trimeric chloride with ROH-pyridine. Liquid, $b_{0.03}$ 170–1°, $n_D^{25.6}$ 1.4473, $d_4^{28.6}$ 1.0342.¹³

(PN(OMe)₂)₃. From trimeric chloride and RNa. Liquid, $b_{0.1}$ 127–8°.¹⁸

The following were prepared by method II, from the trimer.

(PNCl₂)₂(PN(NMe₂)₂). Crystals, m. 98°.¹¹

(PNCl₂)₂(PN(NHCH₂)₂)₂. Crystals, m. 188°.¹¹

(PNCl₂)₂(PN(NH)₂C₆H₄-o). Crystals, m. above 350°.¹¹

(PNCl₂)₂(PN(NH)₂C₆H₃Me-o). Crystals, m. 211°.¹¹

(PNCl₂)₂(PN(NHPh)₂). Crystals, m. 191°.¹¹

(PNCl₂)₂(PN(NHC₆H₄Me-p)₂)₂. Crystals, m. 174°.¹¹

(PN(NHC₆H₄Me-p)₂)₃. Crystals, m. 242°.¹¹

(PN(NC₅H₁₀)₂)₃. Crystals, m. 266° (from EtOH).¹¹

AMIDOPHOSPHITES

(EtO)₂PNHPh. I (from (EtO)₂PCl). Liquid, b_{17} 144–8°, b_{15} 142–4°.¹⁶

(EtO)₂PNHC₁₀H₇-2. I (as above). Liquid, $b_{0.3}$ 126–9°.¹⁶

CHAPTER 11. QUASI-PHOSPHONIUM COMPOUNDS

In a study of hydrolysis of dialkyl fluorophosphates it was found that the reaction is catalyzed by hydrogen ions, thus being unlike the hydrolysis of acyl halides. The reaction is believed, therefore, to go through the intermediate formation of quasi-phosphonium structure.⁵³

CHAPTER 12. DERIVATIVES OF ANHYDRO ACIDS

Although no truly novel reactions suitable for syntheses have been reported, some useful modifications have been applied to the older methods. Thus the synthesis of triphosphates has been improved in the procedure described in Section II. Tertiary bases, notably N-methylmorpholine, give a smooth loss of one benzyl group from the neutral benzyl pyrophosphates, whereas hydrogenation is either ineffective (as in the case of the tetrabenzyl ester), or does not give a homogeneous product.⁷ The reaction is done in refluxing solution with excess base. The condensation of the chlorophosphate with the silver salt to effect the completion of the phosphorus to oxygen to phosphorus link is best done in phenol-acetonitrile solution,⁸ whereas in the synthesis of triphosphates the removal of one benzyl group by N-morpholine is most satisfactorily done in dimethylformamide.⁸ The triphosphates may be prepared by the action of a primary disodium phosphate on a

secondary chlorophosphate used in excess,³⁷ or by the action of a primary dichlorophosphate on dialkyl sodium phosphite used in excess, followed by oxidation of the thus-formed product.³⁸ When the former procedure was used with disilver salt of adenosine-5-phosphate, and the product was de-esterified in the usual manner, the product was identical with the normally unexpected linear triphosphate, having the phosphorus link at the terminal phosphorus atom. The explanation of this apparent rearrangement is yet to be found, although it is believed to involve a cyclization of the initially formed 2-P ester into a monoester of cyclic metaphosphoric acid, followed by ring opening at the site of attachment of the ester link.³⁶

The formation of the pyrophosphate link according to the reactions of Section VIIIA is improved when an excess of trialkyl phosphate is used.³⁹ Lowering of this excess increases the formation of polyphosphates.³⁹ The formation of the pyrophosphates by reactions given in Section XIV may be performed by using the theoretical amount of water under reduced pressure for the removal of deleterious hydrogen halide.³⁸

NEW COMPOUNDS OR NEW CONSTANTS FOR OLDER COMPOUNDS

ACYL PHOSPHATES

BzOPO(OH)₂. II. Silver salt.¹³

(BzO)₂PO(OH). II. Silver salt.¹³

(BzO)(PhO)PO(OH). II. Silver salt.¹⁴

AcOPO(OH)₂. The hydrolysis of the compound was traced by means of O¹⁸. In alkaline media hydrolysis proceeds by cleavage of the Ac group, whereas in acids the AcO group is detached.⁹

PYROPHOSPHATES

Tribenzyl pyrophosphate. II (N-methylmorpholine is used for the debenzylation of the tetrabenzyl ester). The anhydrous compound is a sirup, forming a crystalline monohydrate, m. 65°. The silver salt is sol. in CHCl₃.⁷

(MeO)₂PO·O·PO(OMe)₂. VIIIA. Liquid, b_{0.3} 106–8°. ⁴⁰

(Me₂N)₂PO·O·PO(NMe₂)₂. VIIIA. Liquid, b_{0.002} 98°, b_{0.003} 102°, b_{0.004} 106°, ¹⁷
b₂ 154°, d₂₅²⁵ 1.24.⁴¹

TRIPHOSPHATES

Adenosine-5'-triphosphate. II (either from silver dibenzyl adenosine-5'-pyrophosphate or from disilver adenosine-5'-phosphate). The latter procedure gives a much higher yield.³⁶ Triacridine salt, dec. 209°. ⁸ Acridine salt, which has 2:5 molecular ratio, m. 218° (decomp.).⁸

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INDEX

- Acids, *see* under class names
- Acyl halides, reactions, with phosphates, 334-335
 with phosphine, 14
 with phosphites, 102, 122
- Acyl phosphates, listing of, 348, 349, 368
 preparation of, 334-336
- Acyl phosphites, listing of, 348, 349
 preparation of, 333
- Aldehydes, *see* Carbonyl compounds
 reactions with phosphonium iodide, 15
- Alkali metals, phosphides of, 13
- Alkyl halides, reactions, with phosphites, 121-126
 with sodium phosphides, 13
 with thiophosphates, 234-235
- Alkylphosphorus halides, nomenclature, 4
- Amides, of phosphinous acids, listing of, 304
 nomenclature of, 5
 of phosphonic acids, listing of, 316, 317
 nomenclature of, 5
 preparation of, 279, 280, 289, 297
 of phosphonous acids, listing of, 304
 preparation of, 278
 reactions of, 327
 of phosphoric acid, nomenclature of, 5
 of phosphorous acid, nomenclature of, 5
 of phosphorus acids, pyrolysis of, 282-284
- Amidophosphates, characteristics of, 299, 300
 listing of, 305-316, 366, 367
 preparation of, 279-281, 289, 290, 292-296
- Amidophosphites, listing of, 304
 oxidation of, 289
 preparation of, 278, 279, 286
 reactions, with halides, 289, 327
 with halogens, 288
 with sulfur, 287
- Amidothiophosphates, preparation of, 281, 282
 pyrolysis of, 284, 285
- Amidothiophosphates, listing of, 305-315
 preparation of, 289, 290
- Ammonia, contamination by, 13
- Analysis, physico-chemical, 7
- Anhydro acids, characteristics of, 346-348
 nomenclature of, 6
- Arsinophosphonic acids, listing of, 173, 174
- Basicity, 24
- Biphosphines, listing of, 37, 38
 preparation of, 27, 28
 reactions of, 28
- Bromo-, *see* halo-
- Carbon disulfide, 20, 25, 26
- Carbonyl compounds, 15, 53, 81, 109-111, 129-132, 140, 358-359
- Chloro-, *see* halo-
- Chlorophosphonates, British usage, 6
- Compound tables, arrangement of, 3
- Dealkylation, 232-234, 362, 364
- "Diacytonyl chlorophosphine," structure of, 55, 67, 68, 73
- Dialkylanilines, 20, 49, 50, 109, 135, 136
- Diazoalkanes, 143, 237
- Distillation, inseparable mixtures in, 7
- Esters, of phosphinous acids, nomenclature of, 5
 of phosphonic acids, nomenclature of, 4
 of phosphoric acid, nomenclature of, 5
 of phosphorous acid, nomenclature of, 5
- Ethylene oxide, 14, 126, 127, 230

- Fluoro-, *see* halo-
- Fluorophosphates, toxicity of, 6
- Friedel-Crafts reaction, 43-46, 69, 79, 80, 128, 129, 145
- Grignard reagents, 16, 17, 20-22, 60, 69, 79-82, 105, 107, 108, 132-135, 142, 359
- Haloamidophosphates, alcoholysis of, 287
characteristics of, 298, 299
listing of, 300-303, 366
preparation of, 279-281, 288, 290-293
pyrolysis of, 282-284
reactions of, 287-293
- Haloamidophosphites, listing of, 300
preparation of, 278, 279
- Haloamidothiophosphates, listing of, 303
preparation of, 281, 282, 287, 290, 291
- Halogens, 23, 24, 49-51, 58, 198, 213, 214, 288
- Halophosphates, characteristics of, 237, 238
exchange reactions of, 215
hydrogen bonding in, 238
hydrolysis of, 223-224, 343-344
preparation of, from metaphosphites, 219, 220
from phosphates, 214, 216, 217
from phosphites, 195, 213-215
from phosphorus oxyhalides, 211-213, 216, 217, 226-230
from phosphorus pentachloride, 217, 219, 235
from quasi-phosphonium compounds, 220
from thiophosphates, 220
reactions of, 223-224, 335, 336, 338-340
with diazoalkanes, 143
tabulations of, 240-245, 364
- Halophosphine halides, characteristics of, 70, 71
listing of, 72, 73
nomenclature of, 4
preparation of, from Grignard reagents, 60
from halophosphines, 58-61
from olefins, 59, 127, 128
from phosphine oxides, 59, 60
- Halophosphine halides, pyrolysis of, 70
reactions, with alcohols, 70
with sulfur dioxide, 70
with water, 70
- Halophosphines, alcoholysis of, 52
characteristics of, 51-53
halogen exchange in, 49, 52
hydrolysis of, 12, 52, 137, 138
listing of, 53-56
nomenclature of, 4
oxidation of, 51
preparation of, 42-51
by Friedel-Crafts reaction, 43-46
by pyrolysis, 46, 47, 48, 50
from alkyl halides, 48
from dialkylanilines, 49-50
from mercury compounds, 42-43
from olefins, 48-49
from phosphines, 50-51
from phosphinous acids, 51
from phosphonous acids, 50
reactions, with alcohols, 52
with ammonia bases, 52
with carbonyl compounds, 53, 110-111
with halogens, 51
with hydrogen sulfide, 53
with miscellaneous compounds, 137-140
with organometallic compounds, 52, 53
with oxidizing agents, 51
with sulfur, 51, 52
reduction of, 15
- Halophosphites, characteristics of, 192, 193
hydrolysis of, 188, 189
listing of, 199-200, 362-363
nomenclature of, 5
preparation of, 361-362
from hydroxy compounds, 180-187
reactions of, 192, 193, 215
with sulfur, 215
- Haloselenophosphates, listing of, 245
- Halothiophosphates, hydrolysis of, 224
listing of, 241-245
preparation of, 187, 212, 215-218, 219, 363
- Halothiophosphites, preparation of, 187
- Hydrocarbons, 66, 67, 134, 359

- Hydrogenation, 233, 234
Hydrolysis, 12, 70-71, 137-139, 188-189, 223-224, 232, 233, 235, 343
Hydroxy compounds, 52, 65, 66, 125, 180-187, 191, 192, 212, 217, 218, 229-230, 325-326, 345-346
Hypophosphates, characteristics of, 346
 listing of, 349-350
Hypophosphites, 22, 142
Hypophosphorous acid, reaction with
 carbonyl compounds, 129, 130

Imides, of phosphonous acids, 317
 of phosphoric acid, nomenclature of, 5
 of phosphorous acid, nomenclature of, 5
Imidophosphates, addition reactions of, 327
 listing of, 319-321
 preparation of, 283-285, 295-296
 reactions of, 295-296
Imidophosphites, listing of, 319
 preparation of, 285-286
Imidothiophosphates, listing of, 319-320
Insecticides, 241, 348, 355

Mercury compounds, 42, 43, 80
Metal phosphides, 13
Metaphosphates, listing of, 352
 preparation of, 341, 342
 reactions of, 231-232, 347-348
Metaphosphites, halogenation of, 219-220
 listing of, 351-352
 preparation of, 338-340
Metaphosphonates, listing of, 352
 preparation of, 342
Methylol compounds, 65, 125
Moisture, catalysis by, 6, 181, 182

Nomenclature, 3-6

Olefins, 48, 49, 59, 127-128, 230
Organolithium compounds, 17
Organophosphorus chemistry, pioneer
 work in, 1, 2
 reviews on, 8, 9, 355
Organozinc compounds, 18
Oxidation, 23, 26, 51, 68, 98-99, 100, 193, 196, 198, 236, 239, 289
Oxidation-reduction of phosphonous
 acids, 12

Parachor, 7
Phosphates, *see also* Phosphoric acid,
 esters of
 acid strength, 237-238
 ammonolysis of, 293-294
 applications of, 240-241
 characteristics of, 238-241, 364
 dealkylation of, 232-234, 364
 hydrogenation of, 233-234
 hydrogen bonding in, 238
 hydrolysis of, 232, 233
 listing of, 245-266, 364-365
 nomenclature of, 5
 preparation of, by pyrolysis, 231
 from halophosphates, 223-225, 228, 230-231
 from metal phosphates, 225-226
 from metaphosphates, 231-232
 from olefin oxides, 230
 from olefins, 230
 from phosphites, 227, 231
 from phosphoric acids, 222-223
 from phosphorus pentoxide, 220-222
 from pyrophosphates, 235
 reactions of, 334, 335
 with Grignard reagents, 108
 with unsaturated nitrogen compounds, 237
 with oxidizing agents, 239
 toxicity of, 6
 transesterification in, 227
Phosphinamides, nomenclature of, 5
Phosphine, reactions, with ethylene
 oxide, 14
 with halides, 14
Phosphine-imines, *see* Phosphinimines,
 nomenclature of, 5
Phosphinemethylenes, listing of, 38, 355
 preparation of, 28, 355
 reactions of, 28, 29, 355
Phosphine oxides, characteristics of, 111, 112
 listing of, 113-117, 358
 nomenclature of, 4
 phosphoryl group in, 111-113
 preparation of, by Grignard reaction, 105, 107, 108
 from carbonyl compounds, 109-111
 from dialkylanilines, 109
 from phosphides, 110

- Phosphine oxides, preparation of, from
 phosphines, 98-101
 from phosphine sulfides, 100
 from phosphinites, 102-103
 from phosphonium salts, 104
 from phosphorus, 108-109
 from phosphorus sulfides, 105
 reactions of, 112-113
- Phosphines, 10-41
 addition reactions of, 25, 355
 alkali metal derivatives of, 13
 applications of, 29
 basicity of, 24
 characteristics of, 23-29
 double salts of, 26
 listing of, 30-37
 nomenclature of, 4
 oxidation of, 23, 26, 98-100
 pentacovalent, 27, 355
 preparation of, 10-22
 by Grignard reaction, 16, 17
 by Wurtz reaction, 19
 from aldehydes, 15
 from arsines, 22
 from carbon disulfide, 20
 from dialkylanilines, 20
 from hypophosphites, 22
 from metal derivatives, 12, 13
 from olefin oxides, 14
 from organolithium compounds, 17
 from phosphine, 14, 21
 from phosphonium salts, 10, 11, 12, 18, 19
 from phosphorus, 11, 12
 from phosphorus acids, 12
 from phosphorus sulfides, 20, 21
 pyrolysis of, 29
 reactions of, with alkyl halides, 14, 24, 25
 with Grignard reagents, 22
 with halogens, 23, 24
 with lithium compounds, 27
 with sulfur, 23, 26, 99, 100
 with unsaturated compounds, 26
- Phosphine selenides, listing of, 118
 nomenclature of, 4
- Phosphine sulfides, characteristics of, 111, 113
 listing of, 117, 118
 nomenclature of, 4
- Phosphine sulfides, preparation of, from
 phosphines, 99, 100
 from thiophosphinites, 102, 103
 reactions of, 111, 113
- Phosphinic acids, 6
- Phosphinimines, bond polarity in, 26, 27
 listing of, 317, 318
 nomenclature of, 5
 preparation of, 297
 reactions of, 299
- Phosphinous acids, characteristics of, 144
 listing of, 171, 361
 nomenclature of, 5
 preparation of, 139, 140, 142, 143
- Phosphites, *see also* Phosphorous acid, esters of
 characteristics of, 193-199
 dealkylation of, 362
 hydrolysis of, 188
 listing of, 201-206, 363
 nomenclature of, 5
 preparation of, 180-192
 from hydroxy compounds, 185-187
 from metal phosphites, 189, 190
 from olefin oxides, 185
 from phosphorous acid, 189
 from phosphorus trioxide, 190
 from pyrophosphites, 191
 reactions of, with alcohols, 125, 191, 192
 with Grignard reagents, 17, 108
 with halides, 195-199, 227, 326
 with halogens, 188, 195, 198, 213, 214, 325, 327-328
 with oxidizing agents, 193, 196, 198
 with sulfur, 196
 salts of, 194, 195, 196, 197, 198
 structure of, 193, 194
- Phosphonamides, listing of, 316, 317
 nomenclature of, 5
 preparation of, 279-282, 287, 291, 296
- Phosphonic acids, characteristics of, 143, 144-146
 listing of, 148-171, 360-361
 nomenclature of, 4
 preparation of, by Friedel-Crafts reaction, 128, 129, 145
 by Grignard reaction, 132, 133, 359
 from carbonyl compounds, 129-132, 140

- Phosphonic acids, preparation of, from
dialkylanilines, 135, 136
from hydrocarbons, 134, 359
from methylol compounds, 125
from phosphites, 121-126, 358
from phosphonous acids, 137
from their esters, 125-129, 139, 140,
142, 358, 359
from trivalent derivatives, 121-126,
137, 140
- Phosphonimides, listing of, 321
- Phosphonitrilic chloride, 298, 367
- Phosphonium compounds, *see* Quater-
nary phosphonium compounds
nomenclature of, 4
- Phosphonous acids, characteristics of,
144
esters of, nomenclature of, 5
preparation of, 139, 140
listing of, 146-148, 359, 360
nomenclature of, 5
oxidation-reduction of, 12, 144
preparation of, by Grignard reaction,
142
from halophosphines, 138, 139, 140
from hypophosphites, 126, 142
from nitrogen bases, 135, 136
from olefins, 127, 128
from phosphines, 137
from phosphoryl halides, 138, 139
from unsaturated compounds, 129-
132
- Phosphonyl halides, characteristics of,
70, 71
listing of, 73, 74, 75, 356, 357
nomenclature of, 4
preparation of, by Grignard reaction,
69
from (selected) alcohols, 65
from carbonyl compounds, 67, 68
from halophosphines, 63, 68
from hydrocarbons, 66, 67
from phosphonates, 62, 63, 65
from phosphorus halides, 61, 62
from respective acids, 61, 64
from triarylcarbinols, 64
reactions of, with alcohols, 65, 66, 71
with amines, 71
with phosphonic acids, 71
with water, 70, 71
- Phosphoric acid, esters of, *see also* Phos-
phates
nomenclature of, 5
imides of, nomenclature of, 5
- Phosphorous acid, esters of, *see also*
Phosphites
nomenclature of, 5
imides of, nomenclature of, 5
reaction, with alcohols, 189
with carbonyl compounds, 129, 130
- Phosphorus compounds, trivalent, han-
dling of, 6
- Phosphorus halides, reactions, with al-
cohols, 180-184, 186, 187
with amines, 326-327
with carbonyl compounds, 130-132
with Grignard reagents, 16, 17, 80
with hydrocarbons and oxygen, 66,
67, 356
with olefin oxides, 185-186
with olefins, 59, 356
with phenols, 180-184, 325-326
- Phosphorus pentoxide, reactions, with
alcohols, 345-346
with amines, 295
with hydroxy compounds, 220-222
with oxides and ethers, 341-342
with phosphates, 341
- Phosphorus sulfides, 20, 21, 105, 236,
237, 298, 341, 346
reactions, with alcohols, 346
with nitriles, 298
with thiophosphates, 341
- Polyphosphates, alcoholysis of, 222, 223,
344, 345
hydrolysis of, 343
- Pyrolysis, 29, 46-48, 50, 70, 84, 85, 104,
141, 231, 282, 283, 284, 285, 340-
341, 367, 368
- Pyrophosphates, alkylation of, 337-
338
hydrolysis of, 235
insecticidal, 348
listing of, 350-351, 368
preparation of, 335-341, 343-345, 367-
368
reactions of, 340-341, 346
toxicity of, 6
- Pyrophosphites, 191, 336, 337, 349
- Pyrophosphonates, 351

- Quasi-phosphonium compounds, characteristics of, 220, 328, 329, 367
listing of, 329-332
nomenclature of, 5
preparation of, 325-328
- Quaternary phosphonium compounds, characteristics of, 84-86
listing of, 86-94, 357-358
preparation of, 78-83, 357
from carbonyl compounds, 81
from Grignard reagents, 79, 80, 81, 82
from iodonium salts, 81
from mercury phosphide, 80
from phosphinemethylenes, 83
from phosphines, 78, 79, 82
from phosphine sulfides, 80
from phosphorus, 80, 81, 82
from thiophosphinites, 83
with aluminum chloride, 79, 80
pyrolysis of, 18, 19, 84, 85, 104
reactions of, 18, 19, 83-85
- Refractivity, 7
- Reviews, 8, 9, 355
- Stannaphosphonic acids, listing of, 174
- Sulfur, 4, 5, 6, 23, 26, 287
reactions of, 23, 26, 51, 52, 68, 69, 99, 100, 102, 103, 215, 235-236, 287, 363-364
- Tetraphosphates, 339, 341
- Thiometaphosphates, preparation of, 341
- Thionophosphates, isomerization of, 234-235
nomenclature of, 5
preparation of, 228, 229, 230
- Thionophosphonyl halides, reactions of, 71
- Thionopyrophosphates, preparation of, 345
- Thiophosphates, listing of, 245, 246, 250, 252-254, 256, 257, 258, 259, 260, 262, 263, 264, 265, 266
nomenclature of, 5
oxidation of, 236
preparation of, 235, 236, 237, 363, 364
reactions of, 234, 235, 236, 238
structure of, 238, 239
sulfur removal from, 191
- Thiophosphinous acids, listing of, 171, 172
- Thiophosphites, listing of, 206
- Thiophosphonic acids, listing of, 172, 173
nomenclature of, 4
preparation of, 121, 122, 123, 133, 135, 141
- Thiophosphonous acids, listing of, 172
nomenclature of, 5
- Thiophosphonyl halides, listing of, 75, 357
nomenclature of, 4
preparation of, 68, 69, 356
- Thiophosphoryl chloride, reactions, with hydroxy compounds, 212, 217, 218, 229, 230
with Grignard reagents, 107, 359
- Toxic compounds, 6
- Triaryl carbinols, 64, 125
- Triphosphates, listing of, 351, 368
preparation of, 335, 341, 367, 368
- Wurtz reaction, 19, 136, 289

